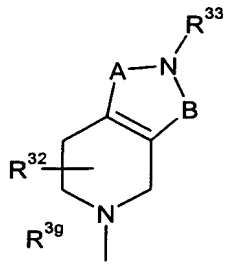
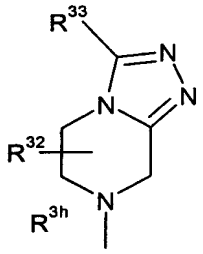
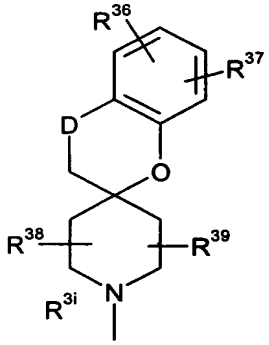
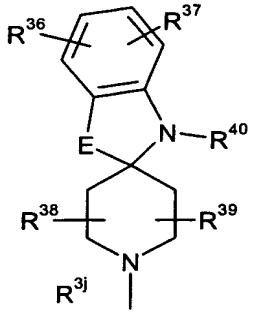
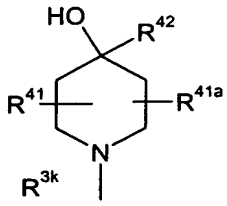
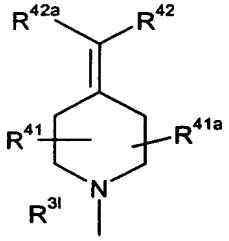
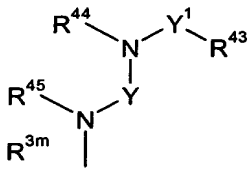
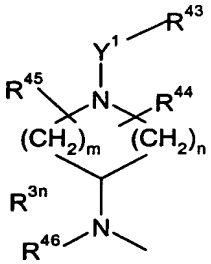
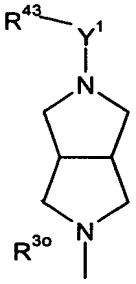
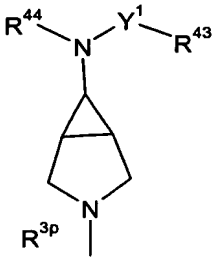
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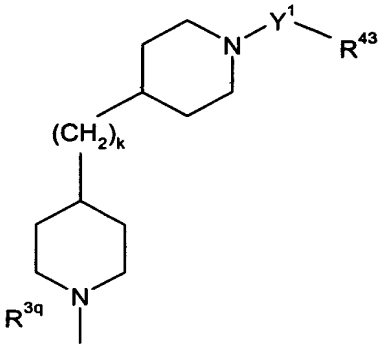

;

wherein said radical of formula R^{3a} is additionally substituted on the ring by R^6, R^7 and R^8;

said radical of formula R^{3b} is additionally substituted on the ring by R^{18}, R^{19} and R^{20};

G, G^1 and G^2 are taken separately and are each hydrogen and R^6 is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; R^7 and R^8 are each independently hydrogen or (C_1-C_4)alkyl; or

G and G^1 are taken together and are (C_1-C_3)alkylene and R^6, R^7, R^8 and G^2 are hydrogen; or

G^1 and G^2 are taken together and are (C_1-C_3)alkylene and R^6, R^7, R^8 and G are hydrogen;

q is 0 or 1;

X is a covalent bond, -(C=NR^{10})-, oxycarbonyl, vinylenylcarbonyl, oxy(C_1-C_4)alkylenylcarbonyl, (C_1-C_4)alkylenylcarbonyl, (C_3-C_4)alkenylcarbonyl, thio(C_1-C_4)alkylenylcarbonyl, vinylenylsulfonyl, sulfinyl-(C_1-C_4)alkylenylcarbonyl, sulfonyl-(C_1-C_4)alkylenylcarbonyl or carbonyl(C_0-C_4)alkylenylcarbonyl; wherein said oxy(C_1-C_4)alkylenylcarbonyl, (C_1-C_4)alkylenylcarbonyl, (C_3-C_4)alkenylcarbonyl and thio(C_1-C_4)alkylenylcarbonyl in the definition of X are each optionally and independently substituted with up to two (C_1-C_4)alkyl, benzyl or Ar; said vinylenylsulfonyl and said vinylenylcarbonyl in the definition of X are optionally substituted independently on one or two vinylenyl carbons with (C_1-C_4)alkyl, benzyl or Ar; and said carbonyl(C_0-C_4)alkylenylcarbonyl in the definition of X is optionally substituted indepedently with up to three (C_1-C_4)alkyl, benzyl or Ar;

R^{10} is hydrogen or (C_1-C_4)alkyl;

R^9 is (C_3-C_7)cycloalkyl, Ar^1-(C_0-C_3)alkylenyl or (C_1-C_6)alkyl optionally substituted with up to five fluoro; provided that when q = 0 and X is a covalent bond, oxycarbonyl or (C_1-C_4)alkylenylcarbonyl, then R^9 is not (C_1-C_6)alkyl;

Ar and Ar^1 are independently a fully saturated, partially saturated or fully unsaturated five- to eight-membered ring optionally having up to four heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or fully unsaturated five- to seven-membered rings, taken independently, optionally having up to four heteroatoms selected independently from nitrogen, sulfur and oxygen, or a tricyclic ring consisting of three fused independently partially saturated, fully saturated or fully unsaturated five to seven membered rings, taken independently, optionally having up

to four heteroatoms selected independently from nitrogen, sulfur and oxygen, said partially saturated, fully saturated ring or fully unsaturated monocyclic ring, bicyclic ring or tricyclic ring optionally having one or two oxo groups substituted on carbon or one or two oxo groups substituted on sulfur;

Ar and Ar^1 are optionally independently substituted on carbon or nitrogen, on one ring if the moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with up to a total of four substituents independently selected from R^{11}, R^{12}, R^{13} and R^{14}; wherein R^{11}, R^{12}, R^{13} and R^{14} are each taken separately and are each independently halo, formyl, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylenyloxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, $C(OH)R^{15}R^{16}$, naphthyl, phenyl, imidazolyl, pyridyl, triazolyl, morpholinyl, (C_0-C_4)alkylsulfamoyl, N-(C_0-C_4)alkylcarbamoyl, N,N-di-(C_1-C_4)alkylcarbamoyl, N-phenylcarbamoyl, N-(C_1-C_4)alkyl-N-phenylcarbamoyl, N,N-diphenyl carbamoyl, (C_1-C_4)alkylcarbonylamido, (C_3-C_7)cycloalkylcarbonylamido, phenylcarbonylamido, piperidinyl, pyrrolidinyl, piperazinyl, cyano, benzimidazolyl, amino, anilino, pyrimidyl, oxazolyl, isoxazolyl, tetrazolyl, thienyl, thiazolyl, benzothiazolyl, pyrrolyl, pyrazolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfanyl, furanyl, 8-(C_1-C_4)alkyl-3,8-diaza[3.2.1]bicyclooctyl, 3,5-dioxo-1,2,4-triazinyl, phenoxy, thiophenoxy, (C_1-C_4)alkylsulfanyl, (C_1-C_4)alkylsulfonyl, (C_3-C_7)cycloalkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said naphthyl, phenyl, pyridyl, piperidinyl, benzimidazolyl, pyrimidyl, thienyl, benzothiazolyl, pyrrolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfanyl, furanyl, thiophenoxy, anilino and phenoxy in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to two substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with up to two substituents independently selected from (C_1-C_4)alkyl; said pyrrolidinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with up to two substituents independently selected from

hydroxy, hydroxy-(C_1-C_3)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with up to three substituents independently selected from (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_3)alkyl, phenyl, pyridyl, (C_0-C_4)alkylsulfamoyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said triazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said tetrazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with hydroxy-(C_2-C_3)alkyl or (C_1-C_4)alkyl optionally substituted with up to five fluoro; and said phenyl and pyridyl which are optionally substituted on piperazine in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; or

R^{11} and R^{12} are taken together on adjacent carbon atoms and are $-CH_2OC(CH_3)_2OCH_2-$ or $-O-(CH_2)_p-O-$, and R^{13} and R^{14} are taken separately and are each independently hydrogen or (C_1-C_4)alkyl;

p is 1, 2 or 3;

R^{15} and R^{16} are taken separately and are each independently hydrogen, (C_1-C_4)alkyl optionally substituted with up to five fluoro; or R^{15} and R^{16} are taken separately and R^{15} is hydrogen and R^{16} is (C_3-C_6)cycloalkyl, hydroxy-(C_1-C_3)alkyl, phenyl, pyridyl, pyrimidyl, thienyl, furanyl, thiazolyl, oxazolyl, imidazolyl, benzothiazolyl or benzoxazolyl; or R^{15} and R^{16} are taken together and are (C_3-C_6)alkylene;

G^3, G^4 and G^5 are taken separately and are each hydrogen; r is 0; R^{18} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; and R^{19} and R^{20} are each independently (C_1-C_4)alkyl; or

G^3, G^4 and G^5 are taken separately and are each hydrogen; r is 1; R^{18} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo,

hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; and R^{19} and R^{20} are each independently hydrogen or (C_1-C_4)alkyl; or

G^3 and G^4 are taken together and are (C_1-C_3)alkylene; r is 0 or 1; and R^{18}, R^{19}, R^{20} and G^5 are hydrogen; or

G^4 and G^5 are taken together and are (C_1-C_3)alkylene; r is 0 or 1; and R^{18}, R^{19}, R^{20} and G^3 are hydrogen;

R^{17} is $SO_2NR^{21}R^{22}$, $CONR^{21}R^{22}$, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylcarbonyl, Ar^2-carbonyl, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkylsulfinyl, Ar^2-sulfonyl, Ar^2-sufinyl and (C_1-C_6)alkyl;

R^{21} and R^{22} are taken separately and are each independently selected from hydrogen, (C_1-C_6)alkyl, (C_3-C_7)cycloalkyl and Ar^2-(C_0-C_4)alkylenyl; or

R^{21} and R^{22} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl, 1,2,3,4-tetrahydro-isoquinolyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{21} and R^{22} is optionally substituted independently with one substituent selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrrolidinyl, piperidinyl, azepinyl in the definition of R^{21} and R^{22} are optionally substituted independently with up to two substituents independently selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{21} and R^{22} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl in the definition of R^{21} and R^{22} is optionally substituted independently with up to three substituents independently selected from phenyl, pyridyl, (C_1-C_4)alkoxycarbonyl and (C_1-C_4)alkyl optionally substituted with up to five fluoro; said 1,2,3,4-tetrahydro-isoquinolyl and said 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl in the definition of R^{21} and R^{22} are optionally substituted independently with up to three substituents independently selected from hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-

C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{21} and R^{22} is optionally substituted with up to four substituents independently selected from hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrimidyl, pyridyl and phenyl which are optionally substituted on said piperazine in the definition of R^{21} and R^{22} is optionally substituted with up to three substituents selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

Ar^2 is independently defined as set forth for Ar and Ar^1 above;

said Ar^2 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{23} is $CONR^{25}R^{26}$ or $SO_2R^{25}R^{26}$, wherein R^{25} is hydrogen (C_1-C_4)alkyl or Ar^3-(C_0-C_4)alkylenyl and R^{26} is Ar^3-(C_0-C_4)alkylenyl; provided that when Ar^3 is phenyl, naphthyl or biphenyl, then R^{23} cannot be $CONR^{25}R^{26}$ where R^{25} is hydrogen or Ar^3 and R^{26} is Ar^3;

R^{24} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro;

Ar^3 is independently defined as set forth for Ar and Ar^1 above;

said Ar^3 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{27} is hydrogen or (C_1-C_4)alkyl;

R^{28} and R^{29} are each independently hydrogen, hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro, (C_1-C_4)alkoxy optionally substituted with up to five fluoro, phenyl, pyridyl, pyrimidyl, thienyl, furanyl, thiazolyl, oxazolyl, phenoxy, thiophenoxy, $SO_2NR^{30}R^{31}$, $CONR^{30}R^{31}$ or $NR^{30}R^{31}$; said thienyl, pyrimidyl, furanyl, thiazolyl and oxazolyl in the definition of R^{28} and R^{29} are optionally substituted by up to two hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said phenyl, pyridyl, phenoxy and thiophenoxy in the definition of R^{28} and R^{29} are optionally substituted by up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-

C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

R^{30} and R^{31} are each independently hydrogen, (C_1-C_4)alkyl, (C_3-C_7)cycloalkyl or phenyl, said phenyl is optionally substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; or

R^{30} and R^{31} are taken together with the nitrogen to which they are attached to form indolinyl, pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl; said pyrrolidinyl and piperidinyl in the definition of R^{30} and R^{31} are optionally substituted with up to two hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said indolinyl and piperazinyl in the definition of R^{30} and R^{31} are optionally substituted with up to three hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{30} and R^{31} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

A is N optionally substituted with hydrogen or (C_1-C_4)alkyl and B is carbonyl; or

A is carbonyl and B is N optionally substituted with hydrogen or (C_1-C_4)alkyl;

R^{32} is hydrogen or (C_1-C_4)alkyl;

R^{33} is phenyl, pyridyl, pyrimidyl, thiazolyl, oxazolyl, benzyl, quinolyl, isoquinolyl, phthalizinyl, quinoxanlyl, benzothiazoyl, benzoxazolyl, benzofuranyl or benzothienyl; said phenyl, pyridyl, pyrimidyl, thiazolyl, oxazolyl, benzyl, quinolyl, isoquinolyl, phthalizinyl, quinoxanlyl, benzothiazoyl, benzoxazolyl, benzofuranyl and benzothienyl in the definition of R^{33} are optionally substituted with up to three phenyl, phenoxy, $NR^{34}R^{35}$, halo, hydroxy, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

R^{34} and R^{35} are each independently hydrogen, (C_1-C_4 alkyl), phenyl or phenylsulfonyl; said phenyl and phenylsulfonyl in the definition of R^{34} and R^{35} are optionally substituted with up to three halo, hydroxy, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

D is CO, CHOH or CH_2;

E is O, NH or S;

R^{36} and R^{37} are taken separately and are each independently hydrogen, halo, cyano, hydroxy, amino, (C_1-C_6)alkylamino, di-(C_1-C_6)alkylamino, pyrrolidino, piperidino, morpholino, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl, Ar^4, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

R^{38}, R^{39} and R^{40} are each independently hydrogen or (C_1-C_4)-alkyl;

Ar^4 is phenyl, furanyl, thienyl, pyridyl, pyrimidyl, pyrazinyl or pyridazinyl; said Ar^4 being optionally substituted with up to three hydroxy, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; or

R^{36} and R^{37} are taken together on adjacent carbon atoms and are -O-$(CH_2)_t$-O-;

t is 1, 2 or 3;

Y is (C_2-C_6)alkylene;

R^{44}, R^{45} and R^{46} are each independently hydrogen or (C_1-C_4)alkyl;

m and n are each independently 1, 2 or 3, provided that the sum of m and n is 2, 3 or 4;

k is 0, 1, 2, 3 or 4;

Y^1 is a covalent bond, carbonyl, sulfonyl or oxycarbonyl;

R^{43} is (C_3-C_7)cycloalkyl, Ar^5-(C_0-C_4)alkylenyl, $NR^{47}R^{48}$ or (C_1-C_6)alkyl optionally substituted with one to five fluoro; provided that when Y^1 is a covalent bond or oxycarbonyl, then R^{43} is not $NR^{47}R^{48}$;

R^{47} and R^{48} are taken separately and are each independently selected from hydrogen, Ar^5, (C_1-C_6)alkyl and Ar^5-(C_0-C_4)alkylenyl; or

R^{47} and R^{48} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 1,2,3,4-tetrahydroisoquinolyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{47} and R^{48} are optionally substituted with one hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrrolidinyl, piperidinyl and azepinyl in the definition of R^{47} and R^{48} are optionally substituted with up to two hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or $(C_1-$

C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{47} and R^{48} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl, 1,2,3,4-tetrahydroisoquinolyl and 5,6,7,8-tetrahydro[4,3-d]pyrimidyl in the definition of R^{47} and R^{48} are optionally substituted with up to three hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{47} and R^{48} are optionally substituted with up to four hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

Ar^5 is independently defined as set forth for Ar and Ar^1 above;

Ar^5 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{42} and R^{42a} are independently hydrogen, (C_3-C_7)cycloalkyl, Ar^6-(C_0-C_3)alkylenyl, Ar^6-(C_2-C_4)alkenyl, Ar^6-carbonyl or (C_1-C_6)alkyl optionally substituted with up to five fluoro;

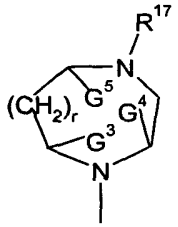
Ar^6 is independently defined as set forth for Ar and Ar^1 above;

Ar^6 is optionally independently substituted as set forth for Ar and Ar^1 above; and

R^{41} and R^{41a} are each independently hydrogen or (C_1-C_4)alkyl.

2. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^3 is



;

substituted by R^{18}, R^{19} or R^{20};

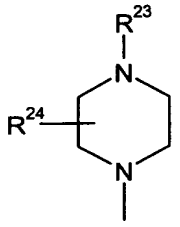
G^3, G^4 and G^5 are taken separately and are each hydrogen, r is 0 and R^{18} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl or phenyl optionally substituted by up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl

optionally substituted with up to five fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; R^{19} and R^{20} are each independently $(C_1$-$C_4)$alkyl;
G^3, G^4 and G^5 are taken separately and are each hydrogen; r is 1; and R^{18} is hydrogen, $(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxycarbonyl or phenyl optionally substituted by up to three hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; R^{19} and R^{20} are each independently hydrogen or $(C_1$-$C_4)$alkyl; or
G^3 and G^4 are taken together and are $(C_1$-$C_3)$alkylene; r is 0 or 1; and R^{18}, R^{19}, R^{20} and G^5 are hydrogen; or
G^4 and G^5 are taken together and are $(C_1$-$C_3)$alkylene; r is 0 or 1; and R^{18}, R^{19}, R^{20} and G^3 are hydrogen;
R^{17} is $SO_2NR^{21}R^{22}$, $CONR^{21}R^{22}$, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkylcarbonyl, Ar^2-carbonyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylsulfinyl, Ar^2-sulfonyl, Ar^2-sufinyl and $(C_1$-$C_6)$alkyl;
R^{21} and R^{22} are taken separately and are each independently selected from hydrogen, $(C_1$-$C_6)$alkyl, $(C_3$-$C_7)$cycloalkyl and Ar^2-$(C_0$-$C_4)$alkylenyl; or
R^{21} and R^{22} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl, 1,2,3,4-tetrahydro-isoquinolyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{21} and R^{22} is optionally substituted independently with one substituent selected from hydroxy, amino, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said pyrrolidinyl, piperidinyl, morpholinyl, azepinyl in the definition of R^{21} and R^{22} are optionally substituted independently with up to two substituents independently selected from hydroxy, amino, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{21} and R^{22} is optionally substituted with up to two substituents independently selected from hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said piperazinyl in the definition of R^{21} and R^{22} is optionally substituted independently with up to three substituents independently selected from phenyl, pyridyl, pyrimidyl, $(C_1$-$C_4)$alkoxycarbonyl and $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro; said

1,2,3,4-tetrahydro-isoquinolyl and said 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl in the definition of R^{21} and R^{22} are optionally substituted independently with up to three substituents independently selected from hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrimidyl, pyridyl and phenyl which are optionally substituted on said piperazine in the definition of R^{21} and R^{22} is optionally substituted with up to three substituents selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{21} and R^{22} is optionally substituted with up to four substituents independently selected from hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro.

3. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^3 is



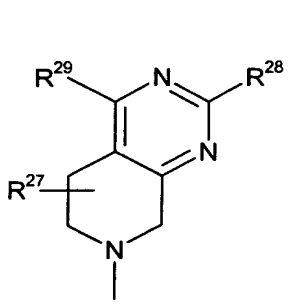
;

R^{23} is $CONR^{25}R^{26}$, $SO_2R^{25}R^{26}$, wherein R^{25} is hydrogen (C_1-C_4)alkyl or Ar^3-(C_0-C_4)alkylenyl and R^{26} is Ar^3-(C_0-C_4)alkylenyl; provided that when Ar^3 is phenyl, naphthyl or biphenyl, then R^{23} cannot be $CONR^{25}R^{26}$ where R^{25} is hydrogen or Ar^3 and R^{26} is Ar^3;

R^{24} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl or phenyl optionally substituted by up to three (C_1-C_4)alkyl optionally substituted with up to five fluoro, (C_1-C_4)alkoxy optionally substituted with up to five fluoro, hydroxy, halo or hydroxy-(C_1-C_3)alkyl.

4. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^3 is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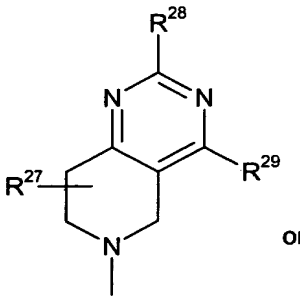
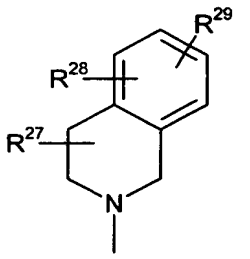

or

,

R^{27} is hydrogen or $(C_1\text{-}C_4)$alkyl;

R^{28} and R^{29} are each independently hydrogen, hydroxy, halo, hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkyl optionally substituted with up to five fluoro, $(C_1\text{-}C_4)$alkoxy optionally substituted with up to five fluoro, phenyl, pyridyl, pyrimidyl, thienyl, furanyl, thiazolyl, oxazolyl, phenoxy, thiophenoxy, $SO_2NR^{30}R^{31}$, $CONR^{30}R^{31}$ or $NR^{30}R^{31}$; said thienyl, pyrimidyl, furanyl, thiazolyl and oxazolyl in the definition of R^{28} and R^{29} are optionally substituted by up to two hydroxy, halo, hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkyl optionally substituted with up to five fluoro or $(C_1\text{-}C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, pyridyl, phenoxy and thiophenoxy in the definition of R^{28} and R^{29} are optionally substituted by up to three hydroxy, halo, hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkyl optionally substituted with up to five fluoro or $(C_1\text{-}C_4)$alkoxy optionally substituted with up to five fluoro;

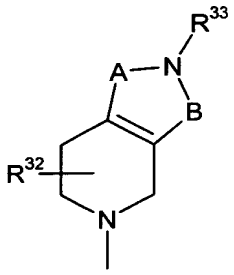
R^{30} and R^{31} are each independently hydrogen, $(C_1\text{-}C_4)$alkyl, $(C_3\text{-}C_7)$cycloalkyl or phenyl, said phenyl is optionally substituted with up to three hydroxy, halo, hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkyl optionally substituted with up to five fluoro or $(C_1\text{-}C_4)$alkoxy optionally substituted with up to five fluoro; or

R^{30} and R^{31} are taken together with the nitrogen to which they are attached to form indolinyl, pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl; said pyrrolidinyl and piperidinyl in the definition of R^{30} and R^{31} are optionally substituted with up to two hydroxy, amino, hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkyl optionally substituted with up to five fluoro or $(C_1\text{-}C_4)$alkoxy optionally substituted with up to five fluoro; said indolinyl and piperazinyl in the definition of R^{30} and R^{31} are optionally substituted with up to three hydroxy, amino, or hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxycarbonyl, $(C_1\text{-}C_4)$alkyl optionally substituted with up to five fluoro or $(C_1\text{-}C_4)$alkoxy optionally substituted with up to five fluoro; and said morpholinyl in the definition of R^{30} and R^{31} is optionally substituted with up to two substituents independently selected from hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1$-

C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro.

5. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^3 is



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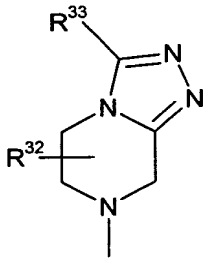
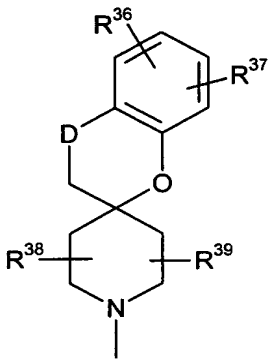


,

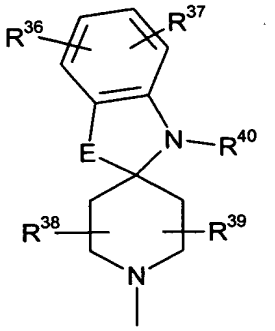
A is N optionally substituted with hydrogen or (C_1-C_4)alkyl and B is carbonyl; or
A is carbonyl and B is N optionally substituted with hydrogen or (C_1-C_4)alkyl;
R^{32} is hydrogen or (C_1-C_4)alkyl;
R^{33} is phenyl, pyridyl, pyrimidyl, thiazolyl, oxazolyl, benzyl, quinolyl, isoquinolyl, phthalizinyl, quinoxanlyl, benzothiazoyl, benzoxazolyl, benzofuranyl or benzothienyl; said phenyl, pyridyl, pyrimidyl, thiazolyl, oxazolyl, benzyl, quinolyl, isoquinolyl, phthalizinyl, quinoxanlyl, benzothiazoyl, benzoxazolyl, benzofuranyl and benzothienyl in the definition of R^{33} are optionally substituted with up to three phenyl, phenoxy, $NR^{34}R^{35}$, halo, hydroxy, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;
R^{34} and R^{35} are each independently hydrogen, (C_1-C_4 alkyl), phenyl or phenylsulfonyl; said phenyl and phenylsulfonyl in the definition of R^{34} and R^{35} are optionally substituted with up to three halo, hydroxy, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro.

6. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^3 is



or



,

D is CO, CHOH or CH_2;

E is O, NH or S;

R^{36} and R^{37} are taken separately and are each independently hydrogen, halo, cyano, hydroxy, amino, $(C_1$-$C_6)$alkylamino, di-$(C_1$-$C_6)$alkylamino, pyrrolidino, piperidino, morpholino, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, hydroxy-$(C_1$-$C_4)$alkyl, Ar^4, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro;

R^{38}, R^{39} and R^{40} are each independently hydrogen or $(C_1$-$C_4)$-alkyl;

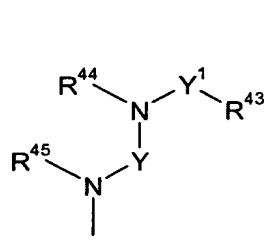
Ar^4 is phenyl, furanyl, thienyl, pyridyl, pyrimidyl, pyrazinyl or pyridazinyl; said Ar^4 being optionally substituted with up to three hydroxy, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; or

R^{36} and R^{37} are taken together on adjacent carbon atoms and are -O-$(CH_2)_t$-O-;

t is 1, 2 or 3.

7. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^3 is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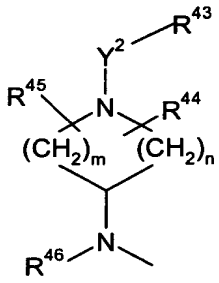
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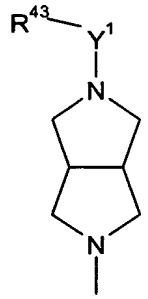
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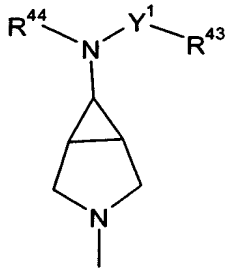
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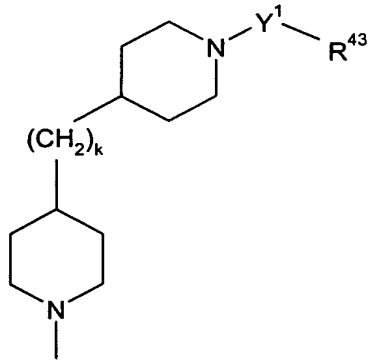

;

Y is $(C_2\text{-}C_6)$alkylene;

R^{44}, R^{45} and R^{46} are each independently hydrogen or $(C_1\text{-}C_4)$alkyl;

m and n are each independently 1, 2 or 3, provided that the sum of m and n is 2, 3 or 4;

k is 0 to 4;

Y^1 is a covalent bond, carbonyl, sulfonyl or oxycarbonyl;

R^{43} is $(C_3\text{-}C_7)$cycloalkyl, $Ar^5\text{-}(C_0\text{-}C_4)$alkylenyl, $NR^{47}R^{48}$ or $(C_1\text{-}C_6)$alkyl optionally substituted with one to five fluoro; provided that when Y^1 is a covalent bond or oxycarbonyl, then R^{43} is not $NR^{47}R^{48}$;

R^{47} and R^{48} are taken separately and are each independently selected from hydrogen, Ar^5, $(C_1\text{-}C_6)$alkyl and $Ar^5\text{-}(C_0\text{-}C_4)$alkylenyl; or

R^{47} and R^{48} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 1,2,3,4-tetrahydroisoquinolyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{47} and R^{48} are optionally substituted with one hydroxy, amino, hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkyl optionally substituted with up to five fluoro or $(C_1\text{-}C_4)$alkoxy optionally substituted with up to five

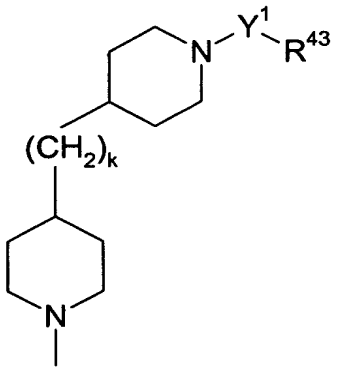
fluoro; said pyrrolidinyl, piperidinyl and azepinyl in the definition of R^{47} and R^{48} are optionally substituted with up to two hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{47} and R^{48} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl, 1,2,3,4-tetrahydroisoquinolyl and 5,6,7,8-tetrahydro[4,3-d]pyrimidyl in the definition of R^{47} and R^{48} are optionally substituted with up to three hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{47} and R^{48} are optionally substituted with up to four hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro.

8. A compound of claim 7, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (R)-1-hydroxy-ethyl;

R^2 is hydrogen;

R^3 is



;

k is 0;

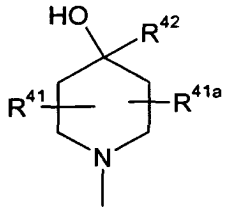
Y^1 is a covalent bond; and

R^{43} is 4-pyrimidinyl substituted at the 2-position with 1-hydroxymethyl.

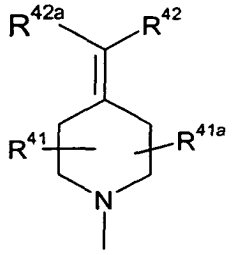
9. The compound of claim 8, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, which is 1R-(4-{1'-[2-(1R-Hydroxy-ethyl)-pyrimidin-4-yl]-[4,4']bipiperidinyl-1-yl}-pyrimidin-2-yl)-ethanol.

10. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^3 is



or



,

R^{42} and R^{42a} are independently hydrogen, $(C_3\text{-}C_7)$cycloalkyl, $Ar^6\text{-}(C_0\text{-}C_3)$alkylenyl, $Ar^6\text{-}(C_2\text{-}C_4)$alkenyl, Ar^6-carbonyl or $(C_1\text{-}C_6)$alkyl optionally substituted with up to five fluoro; and

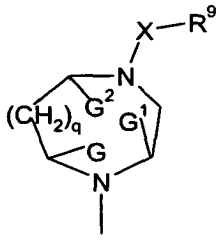
R^{41} and R^{41a} are independently is hydrogen or $(C_1\text{-}C_4)$alkyl.

11. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^1 is $C(OH)R^4R^5$, where R^4 and R^5 are each independently hydrogen or methyl;

R^2 is hydrogen;

R^3 is



,

wherein said R^3 is substituted by R^6, R^7 or R^8;

G, G^1 and G^2 are taken separately and are each hydrogen and R^6 is hydrogen or $(C_1\text{-}C_4)$alkyl; R^7 and R^8 are each independently hydrogen or $(C_1\text{-}C_4)$alkyl; or

G and G^1 are taken together and are $(C_1\text{-}C_3)$alkylene and R^6, R^7, R^8 and G^2 are hydrogen; or

G^1 and G^2 are taken together and are $(C_1\text{-}C_3)$alkylene and R^6, R^7, R^8 and G are hydrogen;

q is 0 or 1;

X is a covalent bond, oxycarbonyl,vinylenylcarbonyl, oxy$(C_1\text{-}C_4)$alkylenylcarbonyl, thio$(C_1\text{-}C_4)$alkylenylcarbonyl or vinylenylsulfonyl; said vinylenylcarbonyl and said vinylenylsulfonyl in the definition of X are optionally substituted on one or two

vinylenyl carbons with (C_1-C_4)alkyl, benzyl or Ar; said oxy(C_1-C_4)alkylenylcarbonyl and said thio(C_1-C_4)alkylenylcarbonyl in the definition of X are optionally substituted with up to two (C_1-C_4)alkyl, benzyl or Ar;

R^9 is (C_3-C_7)cycloalkyl, Ar^1-(C_0-C_4)alkylenyl or (C_1-C_6)alkyl optionally substituted with up to five fluoro;

Ar^1 is phenyl, naphthyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, pteridinyl, pyrazinopyrazinyl, pyrazinopyridazinyl, pyrimidopyridazinyl, pyrimidopyrimidyl, pyridopyrimidyl, pyridopyrazinyl, pyridopyridazinyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, pyrrolopyridyl, furopyridyl, thienopyridyl, imidazolopyridyl, oxazolopyridyl, thiazolopyridyl, pyrazolopyridyl, isoxazolopyridyl, isothiazolopyridyl, pyrrolopyrimidyl, furopyrimidyl, thienopyrimidyl, imidazolopyrimidyl, oxazolopyrimidyl, thiazolopyrimidyl, pyrazolopyrimidyl, isoxazolopyrimidyl, isothiazolopyrimidyl, pyrrolopyrazinyl, furopyrazinyl, thienopyrazinyl, imidazolopyrazinyl, oxazolopyrazinyl, thiazolopyrazinyl, pyrazolopyrazinyl, isoxazolopyrazinyl, isothiazolopyrazinyl, pyrrolopyridazinyl, furopyridazinyl, thienopyridazinyl, imidazolopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl, pyrazolopyridazinyl, isoxazolopyridazinyl or isothiazolopyridazinyl; and

said Ar^1 is optionally substituted as set forth in claim 1.

12. A compound of claim 11, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

X is a covalent bond, oxycarbonyl or vinylenylcarbonyl optionally substituted on one or two vinylenyl carbons with (C_1-C_4)alkyl, benzyl or Ar;

R^9 is Ar^1-(C_0-C_4)alkylenyl;

Ar^1 is phenyl, naphthyl, pyridyl, pyrimidyl, pyrazinyl, triazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, furanyl, thienyl, indolyl, benzofuranyl, benzothienyl, benzoxazolyl, benzothiazolyl, furopyridyl, oxazolopyridyl, thiazolopyridyl, thienopyridyl, furopyrimidyl, thienopyrimidyl, oxazolopyrimidyl or thiazolopyrimidyl; and

said Ar^1 is optionally substituted as set forth in claim 1.

13. A compound of claim 12, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

R^2 is hydrogen;

R^4 is hydrogen or methyl;

R^5 is methyl;

G, G^1 and G^2 are hydrogen;

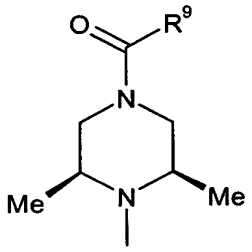
R^6 and R^7 are each independently hydrogen or methyl;

R^8 is hydrogen.

14. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (R)-1-hydroxy-ethyl; and

R^3 is



15. The compound of claim 14, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein: R^9 is 2-furo[3,2-c]pyridyl.

16. The compound of claim 14, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-chloro-furo[3,2-c]pyridyl).

17. The compound of claim 14, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-pyrrolidin-1-yl-furo[3,2-c]pyridyl).

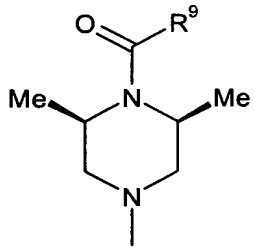
18. The compound of claim 14, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-morpholin-4-yl-furo[3,2-c]pyridyl).

19. The compound of claim 14, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-imidazo[1,2-a]pyridyl.

20. A compound of claim 14, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from furo[3,2-c]pyridin-2-yl-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-methanone; (4-chloro-furo[3,2-c]pyridin-2-yl)-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-methanone; {4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-

dimethyl-piperazin-1-yl}-(4-pyrrolidin-1-yl-furo[3,2-c]pyridin-2-yl)-methanone; {4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-(4-morpholin-4-yl-furo[3,2-c]pyridin-2-yl)-methanone; and {4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-imidazo[1,2-a]pyridin-2-yl-methanone.

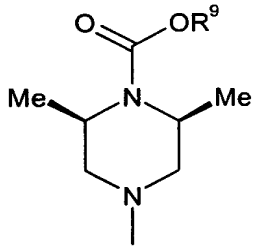
21. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:
R^1 is (R)-1-hydroxy-ethyl; and
R^3 is



22. The compound of claim 21, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-furo[3,2-c]pyridyl.

23. The compound of claim 21, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, which is furo[3,2-c]pyridin-2-yl-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-methanone.

24. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:
R^1 is (R)-1-hydroxy-ethyl; and
R^3 is



25. The compound of claim 24, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 3-pyridyl.

26. The compound of claim 24, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 3-(2-methylpyridyl).

27. The compound of claim 24, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 3-(5-chloropyridyl).

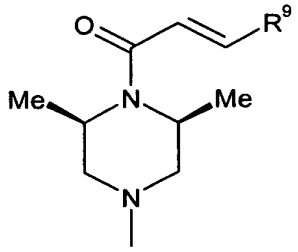
28. The compound of claim 24, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 3-(6-methylpyridyl).

29. A compound of claim 24, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from 4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazine-1-carboxylic acid pyridin-3-yl ester; 4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazine-1-carboxylic acid 2-methyl-pyridin-3-yl ester; 4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazine-1- carboxylic acid 5-chloro-pyridin-3-yl ester; and 4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazine-1-carboxylic acid 6-methyl-pyridin-3-yl ester.

30. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (R)-1-hydroxy-ethyl; and

R^3 is



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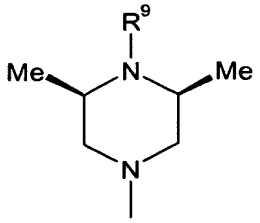
31. The compound of compound of claim 30, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-thienyl.

32. The compound of claim 30, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, which is (E)-1-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-3-thiophen-2-yl-propenone.

33. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (R)-1-hydroxy-ethyl;

R^3 is



; and

R^9 is pyrimidyl or triazinyl; said pyrimidyl or triazinyl is optionally substituted with up to two hydroxy, (C_1-C_4)alkyl, (C_3-C_7)cycloalkyl, (C_1-C_4)alkoxy, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkylenyl, phenyl, piperazinyl optionally substituted with (C_1-C_4)alkyl, or imidazolyl optionally substituted with up to two (C_1-C_4)alkyl.

34. A compound of claim 33, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is pyrimid-2-yl optionally substituted with up to two (C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or (C_1-C_4)alkoxy-(C_1-C_4)alkyl.

35. The compound of claim 34, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4,6-dimethylpyrimid-2-yl.

36. The compound of claim 34, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-methoxymethyl-6-methylpyrimid-2-yl.

37. The compound of claim 34, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-hydroxymethyl-6-methylpyrimid-2-yl.

38. A compound of claim 34, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from1R-{4-[4-(4,6-dimethyl-pyrimidin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-methoxymethyl-6-methyl-pyrimidin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; and 1R-{4-[4-(4-hydroxymethyl-6-methyl-pyrimidin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol.

39. A compound of claim 33, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is pyrimid-4-yl optionally substituted with up to two (C_1-C_4)alkylpiperazin-1-yl or imidazolyl; and said imidazolyl is optionally substituted with up to two (C_1-C_4)alkyl.

40. The compound of claim 39, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-methylpiperazin-1-yl)-pyrimid-4-yl.

41. The compound of claim 39, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-ethylpiperazin-1-yl)- pyrimid-4-yl.

42. The compound of claim 39, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-methylimidazol-1-yl)- pyrimid-4-yl.

43. The compound of claim 39, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(2-methylimidazol-1-yl)- pyrimid-4-yl.

44. The compound of claim 39, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(2,4-dimethylimidazol-1-yl)- pyrimid-4-yl.

45. The compound of claim 39, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-isopropylpiperazin-1-yl)-pyrimid-4-yl.

46. A compound of claim 39, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from 1R-(4-{3R,5S-dimethyl-4-[2-(4-methyl-piperazin-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-(4-{4-[2-(4-ethyl-piperazin-1-yl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-(4-{3R,5S-dimethyl-4-[2-(4-methyl-imidazol-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-(4-{3R,5S-dimethyl-4-[2-(2-methyl-imidazol-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-(4-{4-[2-(2,4-dimethyl-imidazol-1-yl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; and 1R-(4-{4-[2-(4-isopropyl-piperazin-1-yl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol.

47. A compound of claim 33, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is [1,3,5]-triazin-2-yl optionally substituted with up to two (C_1-C_4)alkyl, (C_1-C_4)alkoxy, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkylpiperazin-1-yl or phenyl.

48. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-methyl-6-(4-methylpiperazin-1-yl)-[1,3,5]-triazin-2-yl.

49. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-methoxy-6-methyl-[1,3,5]-triazin-2-yl.

50. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4,6-dimethyoxy-[1,3,5]-triazin-2-yl.

51. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-ethoxy-6-methyl-[1,3,5]-triazin-2-yl.

52. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-isopropoxy-6-methyl-[1,3,5]-triazin-2-yl.

53. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-phenyl-[1,3,5]-triazin-2-yl.

54. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-hydroxymethyl-6-methoxy-[1,3,5]-triazin-2-yl.

55. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-isopropoxy-6-methoxy-[1,3,5]-triazin-2-yl.

56. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-isopropyl-[1,3,5]-triazin-2-yl.

57. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-ethyl-6-methoxy-[1,3,5]-triazin-2-yl.

58. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-cyclopropyl-[1,3,5]-triazin-2-yl.

59. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4,6-dimethyl-[1,3,5]-triazin-2-yl.

60. The compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-methyl-6-phenyl-[1,3,5]-triazin-2-yl.

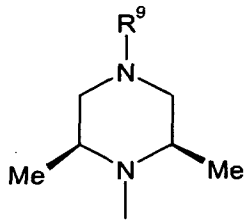
61. A compound of claim 47, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from 1R-(4-{3R,5S-dimethyl-4-[4-methyl-6-(4-methyl-piperazin-1-yl)-[1,3,5]triazin-2-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-{4-[4-(4-methoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4,6-dimethoxy-

[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-ethoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-isopropoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[3R,5S-dimethyl-4-(4-phenyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-hydroxymethyl-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-isopropoxy-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-isopropyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4,6-dimethyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[3R,5S-dimethyl-4-(4-methyl-6-phenyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-cyclopropyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; and 1R-{4-[4-(4-ethyl-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol.

62. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (R)-1-hydroxy-ethyl;

R^3 is



; and

R^9 is pyrimidyl or triazinyl, said pyrimidyl and triazinyl optionally substituted with up to two hydroxy, $(C_1\text{-}C_4)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_1\text{-}C_4)$alkoxy, hydroxy-$(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, triazolyl, acetyl, morpholinyl, $(C_1\text{-}C_4)$alkylpiperazinyl, phenyl or imidazolyl optionally substituted with up to two $(C_1\text{-}C_4)$alkyl.

63. A compound of claim 62, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is pyrimid-2-yl optionally substituted with up to two $(C_1\text{-}C_4)$alkyl, hydroxy-$(C_1\text{-}C_4)$alkyl or triazolyl.

64. The compound of claim 63, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4,6-dimethyl-pyrimid-2-yl.

65. The compound of claim 63, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-hydroxymethyl-6-methylpyrimid-2-yl.

66. The compound of claim 63, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-[1,2,4]-triazol-1-yl-pyrimid-2-yl.

67. A compound of claim 63, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from 1R-{4-[4-(4,6-dimethyl-pyrimidin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]- pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-hydroxymethyl-6-methyl-pyrimidin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; and 1R-{4-[2R,6S-dimethyl-4-(4-[1,2,4]triazol-1-yl-pyrimidin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol.

68. A compound of claim 62, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is pyrimid-4-yl optionally substituted with up to two (C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl, acetyl, morpholinyl, (C_1-C_4)alkylpiperazinyl, triazolyl or imidazolyl optionally substituted with up to two (C_1-C_4)alkyl.

69. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2,6-dimethyl-pyrimid-4-yl.

70. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-hydroxymethyl-6-methyl-pyrimid-4-yl.

71. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-acetyl-pyrimid-4-yl.

72. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-morpholin-4-yl-pyrimid-4-yl.

73. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-methylpiperazin-1-yl)-pyrimid-4-yl.

74. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-[1,2,4]-triazol-1-yl-pyrimid-4-yl.

75. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(1S-hydroxyethyl)-pyrimid-4-yl.

76. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(1R-hydroxyethyl)-pyrimid-4-yl.

77. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-ethylpiperazin-1-yl)-pyrimid-4-yl.

78. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(4-methylimidazol-1-yl)-pyrimid-4-yl.

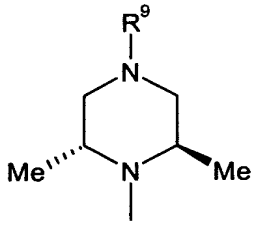
79. The compound of claim 68, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(2,4-dimethylimidazol-1-yl)-pyrimid-4-yl.

80. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from 1R-{4-[4-(2,6-dimethyl-pyrimidin-4-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-{4-[4-(2-hydroxymethyl-6-methyl-pyrimidin-4-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-(4-{4-[2-(1S-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1S-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1-{4-[4-(2-acetyl-pyrimidin-4-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanone; 1RS-(4-{4-[2-(1RS-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; (4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanone; 1R-{4-[2R,6S-dimethyl-4-(2-morpholin-4-yl-pyrimidin-4-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-(4-{2R,6S-dimethyl-4-[2-(4-methyl-piperazin-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-{4-[2R,6S-dimethyl-4-(2-[1,2,4]triazol-1-yl-pyrimidin-4-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6R-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-(4-{4-[2-(4-ethyl-piperazin-1-yl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-(4-{2R,6S-dimethyl-4-[2-(4-methyl-imidazol-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; 1R-{4-[4-(4-cyclopropyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-

ethanol; 1R-{4-[4-(4,6-dimethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-hydroxymethyl-6-phenyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-methoxy-6-methoxymethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[2R,6S-dimethyl-4-(4-methyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl-ethanol; and 1R-(4-{4-[2-(2,4-dimethyl-imidazol-1-yl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol.

81. A compound of claim 13 wherein

R^1 is (R)-1-hydroxyethyl; R^3 is



; and

R^9 is 2-(1R-hydroxyethyl-pyrimid-4-yl, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

82. A compound of claim 62, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein R^9 is [1,3,5]-triazin-2-yl optionally substituted with up to two hydroxy, $(C_1$-$C_4)$alkyl, $(C_3$-$C_7)$cycloalkyl, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy, morpholinyl or phenyl.

83. The compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-morpholin-4-yl-[1,3,5]-triazin-2-yl.

84. The compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-methoxy-6-methyl-[1,3,5]-triazin-2-yl.

85. The compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4,6-dimethoxy-[1,3,5]-triazin-2-yl.

86. A compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-phenyl-[1,3,5]-triazin-2-yl.

87. A compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-cyclopropyl-[1,3,5]-triazin-2-yl.

88. A compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4,6-dimethyl-[1,3,5]-triazin-2-yl.

89. A compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-hydroxymethyl-6-phenyl-[1,3,5]-triazin-2-yl.

90. A compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-methoxy-6-methoxymethyl-[1,3,5]-triazin-2-yl.

91. A compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-methyl-[1,3,5]-triazin-2-yl.

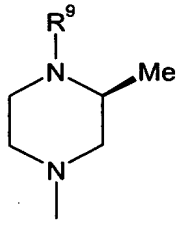
92. A compound of claim 82, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-methoxymethyl-6-phenyl-[1,3,5]triazin-2-yl.

93. The compound of claim 83, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from 1R-{4-[2R,6S-dimethyl-4-(4-morpholin-4-yl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-methoxy-6-methyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4,6-dimethoxy-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(4-methoxymethyl-6-phenyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; and 1R-{4-[2R,6S-dimethyl-4-(4-phenyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol.

94. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (R)-1-hydroxy-ethyl;

R^3 is



; and

R^9 is pyrimidyl, quinoxalyl or oxazolopyridyl optionally substituted with up to two (C_1-C_4)alkyl, (C_1-C_4)alkoxy or hydroxy-(C_1-C_4)alkyl.

95. The compound of claim 94, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 4-hydroxymethyl-6-methyl-pyrimid-2-yl.

96. The compound of claim 94, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-hydroxymethyl-pyrimid-4-yl.

97. The compound of claim 94, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-hydroxymethyl-6-methyl-pyrimid-4-yl.

98. The compound of claim 94, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(oxazolo[5,4-b]pyridyl.

99. The compound of claim 94, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(oxazolo[4,5-b]pyridyl.

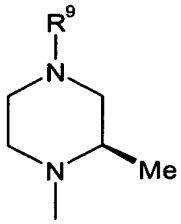
100. The compound of claim 94, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-quinoxalyl.

101. A compound of claim 94, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, selected from 1R-{4-[4-(4-hydroxymethyl-6-methyl-pyrimidin-2-yl)-3S-methyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(2-hydroxymethyl-pyrimidin-4-yl)-3S-methyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol; 1R-{4-[4-(2-hydroxymethyl-6-methyl-pyrimidin-4-yl)-3S-methyl-piperazin-1-yl]-py-rimidin-2-yl}-ethanol; 1R-[4-(3S-methyl-4-oxazolo[5,4-b]pyridin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethanol; 1R-[4-(3S-methyl-4-oxazolo[4,5-b]pyridin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethanol; and 1R-[4-(3S-methyl-4-quinoxalin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethanol.

102. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (R)-1-hydroxy-ethyl;

R^3 is



; and

R^9 is pyrimidyl optionally substituted with up to two $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, hydroxy-$(C_1\text{-}C_4)$alkyl.

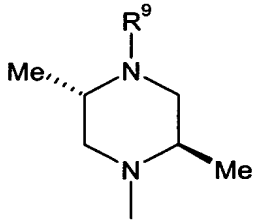
103. The compound of claim 102, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(1R-hydroxyethyl)-pyrimid-4-yl.

104. The compound of claim 102 which is 1R-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R-methyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol.

105. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (R)-1-hydroxy-ethyl;

R^3 is



; and

R^9 is pyrimidyl optionally substituted with up to two $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, hydroxy-$(C_1\text{-}C_4)$alkyl.

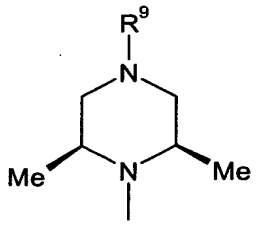
106. The compound of claim 105, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(1R-hydroxyethyl)-pyrimid-4-yl.

107. The compound of claim 105, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, which is (4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol.

108. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is (S)-1-hydroxy-ethyl;

R^3 is



; and

R^9 is pyrimidyl optionally substituted with up to two (C_1-C_4)alkyl, (C_1-C_4)alkoxy or hydroxy-(C_1-C_4)alkyl.

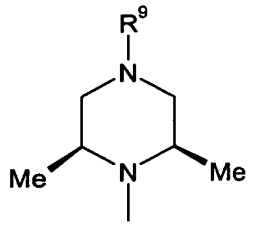
109. The compound of claim 108, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(1R-hydroxy-ethyl)-pyrimid-4-yl.

110. The compound of claim 108, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, which is 1S-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol.

111. A compound of claim 13, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein:

R^1 is acetyl;

R^3 is



; and

R^9 is pyrimidyl optionally substituted with up to two (C_1-C_4)alkyl, (C_1-C_4)alkoxy, acetyl or hydroxy-(C_1-C_4)alkyl.

112. The compound of claim 111, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-acetyl-pyrimid-4-yl.

113. The compound of claim 111, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug wherein: R^9 is 2-(1R-hydroxyethyl)-pyrimid-4-yl.

114. The compound of claim 111 which is 1-{4-[4-(2-acetyl-pyrimidin-4-yl)-2R*,6S*-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanone or 1-(-4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanone.

115. A pharmaceutical composition comprising a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and a pharmaceutically acceptable carrier or diluent.

116. A method of inhibiting sorbitol dehydrogenase in a mammal in need of such inhibition comprising administering to said mammal a sorbitol dehydrogenase inhibiting amount of a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

117. A method of treating diabetes in a mammal suffering from diabetes comprising administering to said mammal an effective amount of a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

118. A method of treating or preventing diabetic complications in a mammal comprising administering to said mammal an effective amount of a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

119. A method of claim 118 wherein said mammal is suffering from diabetes.

120. A method of claim 118 wherein said diabetic complication is diabetic neuropathy.

121. A method of claim 118 wherein said diabetic complication is diabetic nephropathy.

122. A method of claim 118 wherein said diabetic complication is diabetic retinopathy.

123. A method of claim 118 wherein said diabetic complication is foot ulcers.

124. A method of claim 118 wherein said diabetic complication is a cardiovascular condition.

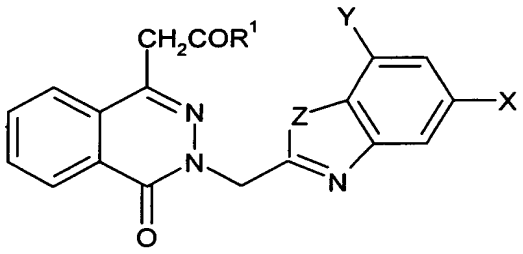
125. A pharmaceutical composition comprising a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and an aldose reductase inhibitor, a prodrug thereof or a pharmaceutically acceptable salt of said aldose reductase inhibitor or said prodrug.

126. A composition of claim 125 additionally comprising a pharmaceutically acceptable carrier or diluent.

127. A composition of claim 126 wherein said aldose reductase inhibitor is selected from the group consisting of ponalrestat, tolrestat, epalrestat, zenarestat, 2R,4R-6,7-dichloro-4-hydroxy-2-methylchroman-4-acetic acid, 2R,4R-6,7-dichloro-6-fluoro-4-hydroxy-2-methylchroman-4-acetic acid, 3,4-dihydro-2,8-diisopropyl-3-oxo-2H-1,4-benzoxazine-4-acetic acid, 3,4-dihydro-3-oxo-4-[(4,5,7-trifluoro-2-benzothiazolyl)methyl]-2H-1,4-benzothiazine-2-acetic acid, N-[3,5-dimethyl-4-[(nitromethyl)sulfonyl]phenyl]-2-methyl-benzeneacetamide, (S)-6-fluorospiro[chroman-4,4′-imidazolidine]-2,5′-dione, d-2-methyl-6-fluoro-spiro(chroman-4′,4′-imidazolidine)-2′,5′-dione, 2-fluoro-spiro(9H-fluorene-

9,4′–imidazolidine)-2′,5′-dione, 2,7-difluoro-spiro(9H-fluorene-9,4′–imidazolidine)-2′,5′-dione, 2,7-difluoro-5-methoxy-spiro(9H-fluorene-9,4'-imidazolidine)-2',5'-dione, 7-fluoro-spiro(5H-indenol[1,2-b]pyridine-5,3′-pyrrolidine)-2,5′-dione, -cis-6′-chloro-2′,3′-dihydro-2′-methyl-spiro-(imidazolidine-4,4′-4′-H-pyrano(2,3-b)pyridine)-2,5-dione, spiro[imidazolidine-4,5′–(6H)-quinoline]-2,5-dione-3′-chloro-7,′8′-dihydro-7′-methyl-(5′-cis), (2S,4S)-6-fluoro-2′,5′-dioxospiro(chroman-4,4′-imidazolidine)-2-carboxamide, and 2-[(4-bromo-2-fluorophenyl)methyl]-6-fluorospiro[isoquinoline-4-(1H),3′-pyrrolidine]-1,2′,3,5′(2H)-tetrone.

128. A composition of claim 126 wherein said aldose reductase inhibitor is selected from the group consisting of compounds of the formula ARI,



ARI

or a pharmaceutically acceptable salt thereof, wherein

Z in the compound of formula ARI is O or S;

R^1 in the compound of formula ARI is hydroxy or a group capable of being removed in vivo to produce a compound of formula ARI wherein R^1 is OH; and

X and Y in the compound of formula ARI are the same or different and are selected from hydrogen, trifluoromethyl, fluoro, and chloro.

129. A composition of claim 128 wherein said aldose reductase inhibitor is selected from the group consisting of 3,4-dihydro-3-(5-fluorobenzothiazol-2-ylmethyl)-4-oxophthalazin-1-yl-acetic acid, 3-(5,7-difluorobenzothiazol-2-ylmethyl)-3,4-dihydro-4-oxophthalazin-1-ylacetic acid, 3-(5-chlorobenzothiazol-2-ylmethyl)-3,4-dihydro-4-oxophthalazin-1-ylacetic acid, 3-(5,7-dichlorobenzothiazol-2-ylmethyl)-3,4-dihydro-4-oxophthalazin-1-ylacetic acid, 3,4-dihydro-4-oxo-3-(5-trifluoromethylbenzoxazol-2-ylmethyl)phthalazin-1-ylacetic acid, 3,4-dihydro-3-(5-fluorobenzoxazol-2-ylmethyl)-4-oxophthalazin-1-yl-acetic acid, 3-(5,7-difluorobenzoxazol-2-ylmethyl)-3,4-dihydro-4-oxophthalazin-1- ylacetic acid, 3-(5-chlorobenzoxazol-2-ylmethyl)-3,4-dihydro-4-oxophthalazin-1-ylacetic acid, 3-(5,7-dichlorobenzoxazol-2-ylmethyl)-3,4-dihydro-4-oxophthalazin-1- ylacetic acid, and zopolrestat.

130. A method of treating diabetes in a mammal suffering from diabetes comprising administering to said mammal an effective amount of a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and an aldose reductase inhibitor, a prodrug of said aldose reductase inhibitor or a pharmaceutically acceptable salt of said aldose reductase inhibitor or said prodrug.

131. A method of treating or preventing diabetic complications in a mammal comprising administering to said mammal an effective amount of a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable of said compound or said prodrug and an aldose reductase inhibitor, a prodrug of said aldose reductase inhibitor or a pharmaceutically acceptable salt of said aldose reductase inhibitor or said prodrug thereof.

132. A method of claim 131 wherein said mammal is suffering from diabetes.

133. A method of claim 131 wherein said diabetic complication is diabetic neuropathy.

134. A method of claim 131 wherein said diabetic complication is diabetic nephropathy.

135. A method of claim 131 wherein said diabetic complication is diabetic retinopathy.

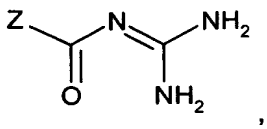
136. A method of claim 131 wherein said diabetic complication is foot ulcers.

137. A method of claim 131 wherein said diabetic complication is a cardiovascular condition.

138. A pharmaceutical composition comprising a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and a sodium hydrogen ion exchange (NHE-1) inhibitor, a prodrug of said NHE-1 inhibitor or a pharmaceutically acceptable salt of said NHE-1 inhibitor or said prodrug thereof.

139. A composition of claim 138 additionally comprising a pharmaceutically acceptable carrier or diluent.

140. A composition of claim 138 wherein said NHE-1 inhibitor is a compound of the formula NHE,



NHE

a prodrug thereof or a pharmaceutically acceptable salt of said compound or of said prodrug, wherein

Z in the compound of formula NHE is carbon connected and is a five-membered, diaza, diunsaturated ring having two contiguous nitrogens, said ring optionally mono-, di-, or tri-substituted with up to three substituents independently selected from R^1, R^2 and R^3 ;

or

Z in the compound of formula NHE carbon connected and is a five-membered, triaza, diunsaturated ring, said ring optionally mono- or di-substituted with up to two substituents independently selected from R^4 and R^5;

wherein R^1, R^2, R^3, R^4 and R^5 in the compound of formula NHE are each independently hydrogen, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl, (C_1-C_4)alkylthio, (C_3-C_4)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkoxy(C_1-C_4)alkyl, mono-N- or di-N,N-(C_1-C_4)alkylcarbamoyl, M or M(C_1-C_4)alkyl, any of said previous (C_1-C_4)alkyl moieties optionally having from one to nine fluorines; said (C_1-C_4)alkyl or (C_3-C_4)cycloalkyl optionally mono-or di-substituted independently with hydroxy, (C_1-C_4)alkoxy, (C_1-C_4)alkylthio, (C_1-C_4)alkylsulfinyl, (C_1-C_4)alkylsulfonyl, (C_1-C_4)alkyl, mono-N- or di-N,N-(C_1-C_4)alkylcarbamoyl or mono-N- or di-N,N-(C_1-C_4)alkylaminosulfonyl; and said (C_3-C_4)cycloalkyl optionally having from one to seven fluorines;

wherein M in the compound of formula NHE is a partially saturated, fully saturated or fully unsaturated five to eight membered ring optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen, or, a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen;

said M in the compound of formula NHE is optionally substituted, on one ring if the moiety is monocyclic, or one or both rings if the moiety is bicyclic, on carbon or nitrogen with up to three substituents independently

selected from R^6, R^7 and R^8, wherein one of R^6, R^7 and R^8 is optionally a partially saturated, fully saturated, or fully unsaturated three to seven membered ring optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen optionally substituted with $(C_1$-$C_4)$alkyl and additionally R^6, R^7 and R^8 are optionally hydroxy, nitro, halo, $(C_1$-$C_4)$alkoxy, $(C_1$-$C_4)$alkoxycarbonyl, $(C_1$-$C_4)$alkyl, formyl, $(C_1$-$C_4)$alkanoyl, $(C_1$-$C_4)$alkanoyloxy, $(C_1$-$C_4)$alkanoylamino, $(C_1$-$C_4)$alkoxycarbonylamino, sulfonamido, $(C_1$-$C_4)$alkylsulfonamido, amino, mono-N- or di-N,N-$(C_1$-$C_4)$alkylamino, carbamoyl, mono-N- or di-N,N-$(C_1$-$C_4)$alkylcarbamoyl, cyano, thiol, $(C_1$-$C_4)$alkylthio, $(C_1$-$C_4)$alkylsulfinyl, $(C_1$-$C_4)$alkylsulfonyl, mono-N- or di-N,N-$(C_1$-$C_4)$alkylaminosulfonyl, $(C_2$-$C_4)$alkenyl, $(C_2$-$C_4)$alkynyl or $(C_5$-$C_7)$cycloalkenyl,

wherein said $(C_1$-$C_4)$alkoxy, $(C_1$-$C_4)$alkyl, $(C_1$-$C_7)$alkanoyl, $(C_1$-$C_4)$alkylthio, mono-N- or di-N,N-$(C_1$-$C_4)$alkylamino or $(C_3$-$C_7)$cycloalkyl R^6, R^7 and R^8 substituents are optionally mono- substituted independently with hydroxy, $(C_1$-$C_4)$alkoxycarbonyl, $(C_3$-$C_7)$cycloalkyl, $(C_1$-$C_4)$alkanoyl, $(C_1$-$C_4)$alkanoylamino, $(C_1$-$C_4)$alkanoyloxy, $(C_1$-$C_4)$alkoxycarbonylamino, sulfonamido, $(C_1$-$C_4)$alkylsulfonamido, amino, mono-N- or di-N,N-$(C_1$-$C_4)$alkylamino, carbamoyl, mono-N- or di-N,N-$(C_1$-$C_4)$alkylcarbamoyl, cyano, thiol, nitro, $(C_1$-$C_4)$alkylthio, $(C_1$-$C_4)$alkylsulfinyl, $(C_1$-$C_4)$alkylsulfonyl or mono- N- or di-N,N-$(C_1$-$C_4)$alkylaminosulfonyl or optionally substituted with one to nine fluorines.

141. A composition of claim 140 wherein said NHE-1 inhibitor is selected from the group consisting of [1-(8-bromoquinolin-5-yl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(6-chloroquinolin-5-yl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine; [1-(indazol-7-yl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(benzimidazol-5-yl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(1-isoquinolyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[5-cyclopropyl-1-(4-quinolinyl)-1*H*-pyrazole-4-carbonyl]guanidine;
[5-cyclopropyl-1-(quinolin-5-yl)-1H-pyrazole-4-carbonyl]guanidine;
[5-cyclopropyl-1-(quinolin-8-yl)-1H-pyrazole-4-carbonyl]guanidine;
[1-(indazol-6-yl)-5-ethyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(indazol-5-yl)-5-ethyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(benzimidazol-5-yl)-5-ethyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(1-methylbenzimidazol-6-yl)-5-ethyl-1*H*-pyrazole-4-carbonyl]guanidine;

1-(5-quinolinyl)-5-*n*-propyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(5-quinolinyl)-5-isopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[5-ethyl-1-(6-quinolinyl)-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-methylbenzimidazol-5-yl)-5-ethyl-1*H*-pyrazole-4-carbonyl]guanidine; [1-(1,4-benzodioxan-6-yl)-5-ethyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(benzotriazol-5-yl)-5-ethyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(3-chloroindazol-5-yl)-5-ethyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(5-quinolinyl)-5-butyl-1*H*-pyrazole-4-carbonyl]guanidine;
[5-propyl-1-(6-quinolinyl)-1*H*-pyrazole-4-carbonyl]guanidine;
[5-isopropyl-1-(6-quinolinyl)-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-chloro-4-methylsulfonylphenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-chlorophenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-trifluoromethyl-4-fluorophenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-bromophenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-fluorophenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-chloro-5-methoxyphenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-chloro-4-methylaminosulfonylphenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2,5-dichlorophenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2,3-dichlorophenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-chloro-5-aminocarbonylphenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-chloro-5-aminosulfonylphenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-fluoro-6-trifluoromethylphenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-chloro-5-methylsulfonylphenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-chloro-5-dimethylaminosulfonylphenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;
[1-(2-trifluoromethyl-4-chlorophenyl)-5-cyclopropyl-1*H*-pyrazole-4-carbonyl]guanidine;

[1-(2-chlorophenyl)-5-methyl-1H-pyrazole-4-carbonyl]guanidine;
[5-methyl-1-(2-trifluoromethylphenyl)-1H-pyrazole-4-carbonyl]guanidine;
[5-ethyl-1-phenyl-1H-pyrazole-4-carbonyl]guanidine;
[5-cyclopropyl-1-(2-trifluoromethylphenyl)-1H-pyrazole-4-carbonyl]guanidine;
[5-cyclopropyl-1-phenyl-1H-pyrazole-4-carbonyl]guanidine;
[5-cyclopropyl-1-(2,6-dichlorophenyl)-1H-pyrazole-4-carbonyl]guanidine; or a pharmaceutically acceptable salt thereof.

142. A method of treating ischemia in a mammal suffering from ischemia comprising administering to said mammal an effective amount of a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and a sodium hydrogen ion exchange (NHE-1) inhibitor, a prodrug of said NHE-1 inhibitor or a pharmaceutically acceptable salt of said NHE-1 inhibitor or said prodrug.

143. A method of claim 142 wherein said ischemia is perioperative myocardial ischemia.

144. A method of treating or preventing diabetic complications in a mammal comprising administering to said mammal an effective amount of a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and a sodium hydrogen ion exchange (NHE-1) inhibitor, a prodrug of said NHE-1 inhibitor or a pharmaceutically acceptable salt of said NHE-1 inhibitor or said prodrug.

145. A method of claim 144 wherein said mammal is suffering from diabetes.

146. A method of claim 144 wherein said diabetic complication is diabetic neuropathy.

147. A method of claim 144 wherein said diabetic complication is diabetic nephropathy.

148. A method of claim 144 wherein said diabetic complication is diabetic retinopathy.

149. A method of claim 144 wherein said diabetic complication is foot ulcers.

150. A method of claim 144 wherein said diabetic complication is a cardiovascular condition.

151. A method of treating diabetes in a mammal suffering from diabetes comprising administering to said mammal an effective amount of a compound of

claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, and a sodium hydrogen ion exchange (NHE-1) inhibitor, a prodrug of said NHE-1 inhibitor or a pharmaceutically acceptable salt of said NHE-1 inhibitor or said prodrug.

152. A kit comprising:

a. a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug in a first unit dosage form;

b. an aldose reductase inhibitor, a prodrug thereof or a pharmaceutically acceptable salt of said prodrug or said aldose reductase inhibitor in a second unit dosage form; and

c. a container.

153. A kit comprising:

a. a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug in a first unit dosage form;

b. a sodium hydrogen ion exchange (NHE-1) inhibitor, a prodrug thereof or a pharmaceutically acceptable salt of said prodrug or said NHE-1 inhibitor in a second unit dosage form; and

c. a container.

154. A method of inhibiting sorbitol dehydrogenase in a mammal in need thereof comprising administering to said mammal a pharmaceutical composition of claim 115.

155. A method of treating ischemia in a mammal suffering from ischemia comprising administering to said mammal a pharmaceutical composition of claim 138.

156. A method of claim 154 wherein said ischemia is perioperative myocardial ischemia.

157. A method of treating or preventing diabetic complications in a mammal comprising administering to said mammal a pharmaceutical composition of claim 115.

158. A method of claim 157 wherein said mammal is suffering from diabetes.

159. A method of treating or preventing diabetic complications in a mammal comprising administering to said mammal a pharmaceutical composition of claim 125.

160. A method of claim 159 wherein said mammal is suffering from diabetes.

161. A method of treating or preventing diabetic complications in a mammal comprising administering to said mammal a pharmaceutical composition of claim 138.

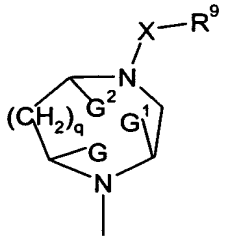
162. A method of claim 161 wherein said mammal is suffering from diabetes.

163. A compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug, wherein:

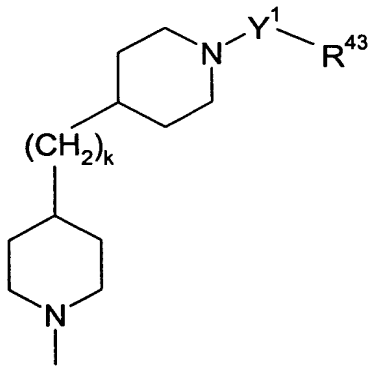
R^1 is $C(OH)R^4R^5$, where R^4 and R^5 are each independently hydrogen or methyl;

R^2 is hydrogen;

R^3 is



or



;

wherein said piperazinyl R^3 is substituted by R^6, R^7 or R^8;

G, G^1 and G^2 are taken separately and are each hydrogen and R^6 is hydrogen or $(C_1\text{-}C_4)$alkyl; R^7 and R^8 are each independently hydrogen or $(C_1\text{-}C_4)$alkyl; or

G and G^1 are taken together and are $(C_1\text{-}C_3)$alkylene and R^6, R^7, R^8 and G^2 are hydrogen; or

G^1 and G^2 are taken together and are $(C_1\text{-}C_3)$alkylene and R^6, R^7, R^8 and G are hydrogen;

q is 0 or 1;

X is a covalent bond, oxycarbonyl,vinylenylcarbonyl, oxy$(C_1\text{-}C_4)$alkylenylcarbonyl, thio$(C_1\text{-}C_4)$alkylenylcarbonyl or vinylenylsulfonyl; said vinylenylcarbonyl and said vinylenylsulfonyl in the definition of X are optionally substituted on one or two vinylenyl carbons with $(C_1\text{-}C_4)$alkyl, benzyl or Ar; said oxy$(C_1\text{-}C_4)$alkylenylcarbonyl

and said thio(C_1-C_4)alkylenylcarbonyl in the definition of X are optionally substitut d with up to two (C_1-C_4)alkyl, benzyl or Ar;

R^9 is (C_3-C_7)cycloalkyl, Ar^1-(C_0-C_4)alkylenyl or (C_1-C_6)alkyl optionally substituted with up to five fluoro;

Ar^1 is phenyl, naphthyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, pteridinyl, pyrazinopyrazinyl, pyrazinopyridazinyl, pyrimidopyridazinyl, pyrimidopyrimidyl, pyridopyrimidyl, pyridopyrazinyl, pyridopyridazinyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, pyrrolopyridyl, furopyridyl, thienopyridyl, imidazolopyridyl, oxazolopyridyl, thiazolopyridyl, pyrazolopyridyl, isoxazolopyridyl, isothiazolopyridyl, pyrrolopyrimidyl, furopyrimidyl, thienopyrimidyl, imidazolopyrimidyl, oxazolopyrimidyl, thiazolopyrimidyl, pyrazolopyrimidyl, isoxazolopyrimidyl, isothiazolopyrimidyl, pyrrolopyrazinyl, furopyrazinyl, thienopyrazinyl, imidazolopyrazinyl, oxazolopyrazinyl, thiazolopyrazinyl, pyrazolopyrazinyl, isoxazolopyrazinyl, isothiazolopyrazinyl, pyrrolopyridazinyl, furopyridazinyl, thienopyridazinyl, imidazolopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl, pyrazolopyridazinyl, isoxazolopyridazinyl or isothiazolopyridazinyl; and

said Ar^1 is optionally substituted as set forth above;

k is 0, 1, 2, 3 or 4;

Y^1 is a covalent bond, carbonyl, sulfonyl or oxycarbonyl;

R^{43} is (C_3-C_7)cycloalkyl, Ar^5-(C_0-C_4)alkylenyl, $NR^{47}R^{48}$ or (C_1-C_6)alkyl optionally substituted with one to five fluoro; provided that when Y^1 is a covalent bond or oxycarbonyl, then R^{43} is not $NR^{47}R^{48}$;

R^{47} and R^{48} are taken separately and are each independently selected from hydrogen, Ar^5, (C_1-C_6)alkyl and Ar^5-(C_0-C_4)alkylenyl; or

R^{47} and R^{48} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 1,2,3,4-tetrahydroisoquinolyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{47} and R^{48} are optionally substituted with one hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to

fluoro; said pyrrolidinyl, piperidinyl and azepinyl in the definition of R^{47} and R^{48} are optionally substituted with up to two hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{47} and R^{48} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl, 1,2,3,4-tetrahydroisoquinolyl and 5,6,7,8-tetrahydro[4,3-d]pyrimidyl in the definition of R^{47} and R^{48} are optionally substituted with up to three hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{47} and R^{48} are optionally substituted with up to four hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

Ar^5 is independently defined as set forth for Ar and Ar^1 above;

Ar^5 is optionally independently substituted as set forth for Ar and Ar^1 above.

164. A compound selected from

1R-(4-{1'-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-[4,4']bipiperidinyl-1-yl}-pyrimidin-2-yl)-ethanol;

furo[3,2-c]pyridin-2-yl-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-methanone;

(4-chloro-furo[3,2-c]pyridin-2-yl)-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-methanone;

{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-(4-pyrrolidin-1-yl-furo[3,2-c]pyridin-2-yl)-methanone;

{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-(4-morpholin-4-yl-furo[3,2-c]pyridin-2-yl)-methanone;

{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-imidazo[1,2-a]pyridin-2-yl-methanone;

furo[3,2-c]pyridin-2-yl-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-methanone;

4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazine-1-carboxylic acid pyridin-3-yl ester;

4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazine-1-carboxylic acid 2-methyl-pyridin-3-yl ester;

4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazine-1- carboxylic acid 5-chloro-pyridin-3-yl ester;

4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazine-1-carboxylic acid 6-methyl-pyridin-3-yl ester;

(E)-1-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-3-thiophen-2-yl-propenone;

1R-{4-[4-(4,6-dimethyl-pyrimidin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;

1R-{4-[4-(4-methoxymethyl-6-methyl-pyrimidin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;

1R-{4-[4-(4-hydroxymethyl-6-methyl-pyrimidin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;

1R-(4-{3R,5S-dimethyl-4-[2-(4-methyl-piperazin-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;

1R-(4-{4-[2-(4-ethyl-piperazin-1-yl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;

1R-(4-{3R,5S-dimethyl-4-[2-(4-methyl-imidazol-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;

1R-(4-{3R,5S-dimethyl-4-[2-(2-methyl-imidazol-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;

1R-(4-{4-[2-(2,4-dimethyl-imidazol-1-yl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;

1R-(4-{4-[2-(4-isopropyl-piperazin-1-yl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;

1R-(4-{3R,5S-dimethyl-4-[4-methyl-6-(4-methyl-piperazin-1-yl)-[1,3,5]triazin-2-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;

1R-{4-[4-(4-methoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;

1R-{4-[4-(4,6-dimethoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;

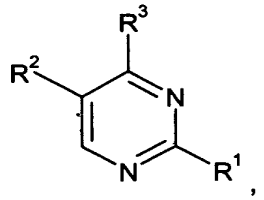
1R-{4-[4-(4-ethoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;

1R-{4-[4-(4-isopropoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[3R,5S-dimethyl-4-(4-phenyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-hydroxymethyl-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-isopropoxy-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-isopropyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-ethyl-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4,6-dimethyl-pyrimidin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]- pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-hydroxymethyl-6-methyl-pyrimidin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[2R,6S-dimethyl-4-(4-[1,2,4]triazol-1-yl-pyrimidin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(2,6-dimethyl-pyrimidin-4-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
1R-{4-[4-(2-hydroxymethyl-6-methyl-pyrimidin-4-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-(4-{4-[2-(1S-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
1S-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
1-{4-[4-(2-acetyl-pyrimidin-4-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanone;
1RS-(4-{4-[2-(1RS-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanone;

1R-{4-[2R,6S-dimethyl-4-(2-morpholin-4-yl-pyrimidin-4-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-(4-{2R,6S-dimethyl-4-[2-(4-methyl-piperazin-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
1R-{4-[2R,6S-dimethyl-4-(2-[1,2,4]triazol-1-yl-pyrimidin-4-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6R-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
1R-(4-{4-[2-(4-ethyl-piperazin-1-yl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
1R-(4-{2R,6S-dimethyl-4-[2-(4-methyl-imidazol-1-yl)-pyrimidin-4-yl]-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
1R-(4-{4-[2-(2,4-dimethyl-imidazol-1-yl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol;
1R-{4-[2R,6S-dimethyl-4-(4-morpholin-4-yl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-methoxy-6-methyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4,6-dimethoxy-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[2R,6S-dimethyl-4-(4-phenyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-hydroxymethyl-6-methyl-pyrimidin-2-yl)-3S-methyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(2-hydroxymethyl-pyrimidin-4-yl)-3S-methyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(2-hydroxymethyl-6-methyl-pyrimidin-4-yl)-3S-methyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-[4-(3S-methyl-4-oxazolo[5,4-b]pyridin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethanol;
1R-[4-(3S-methyl-4-oxazolo[4,5-b]pyridin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethanol;
1R-[4-(3S-methyl-4-quinoxalin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethanol;
1R-{4-[4-(4,6-dimethyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[3R,5S-dimethyl-4-(4-methyl-6-phenyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]pyrimidin-2-yl}-ethanol;

1R-{4-[4-(4-cyclopropyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-cyclopropyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4,6-dimethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-hydroxymethyl-6-phenyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[4-(4-methoxy-6-methoxymethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
1R-{4-[2R,6S-dimethyl-4-(4-methyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl-ethanol;
1-{4-[4-(2-acetyl-pyrimidin-4-yl)-2R*,6S*-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanone;
1-(-4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanone;
1R-{4-[4-(4-methoxymethyl-6-phenyl-[1,3,5]-triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethanol;
(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol; and
1S-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethanol.

165. A compound of the formula I^A,



I^A

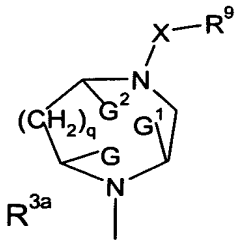
wherein:

R^1 is C-(OR^{80})R^4R^5, where R^{80} is independently (C_1-C_4)alkyl, benzyl, (C_1-C_6)alkylcarbonyl or phenylcarbonyl, where said benzyl and said phenyl are optionally substituted with up to three (C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo or nitro;

R^4 and R^5 are each independently hydrogen, methyl, ethyl or hydroxy-(C_1-C_3)alkyl;

R^2 is hydrogen, (C_1-C_4)alkyl or (C_1-C_4)alkoxy;

R^3 is a radical of the formula



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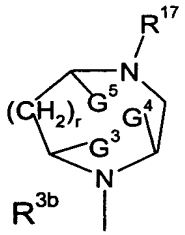

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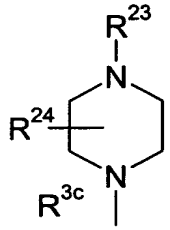

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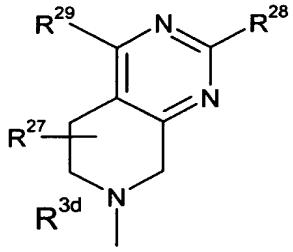

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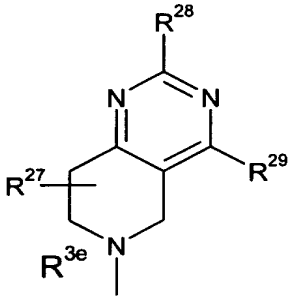

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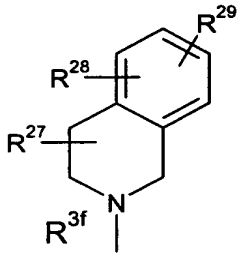

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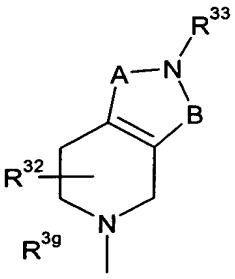

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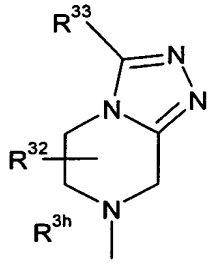

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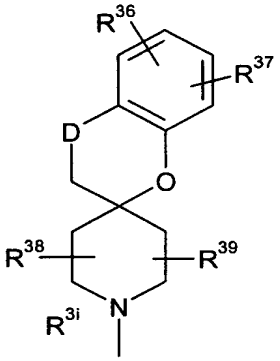

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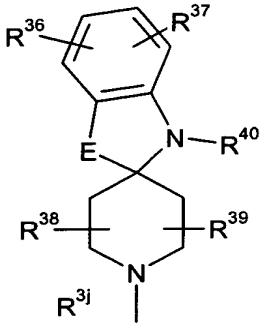

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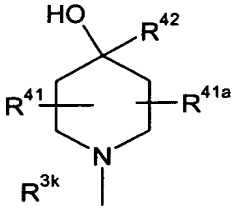

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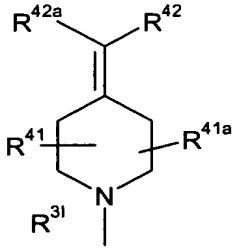

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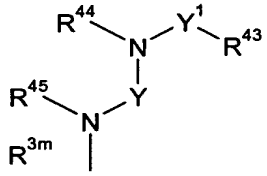

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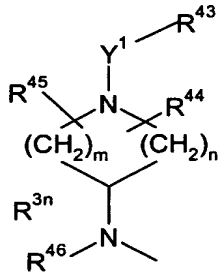

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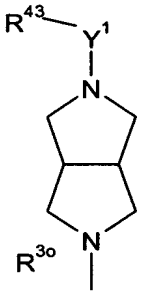

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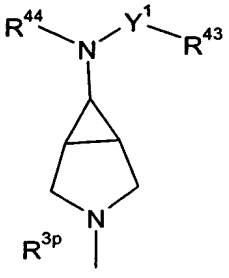

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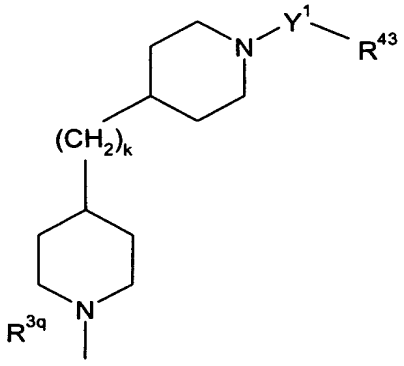


;

wherein said radical of formula R^{3a} is substituted by R^6, R^7 and R^8;

said radical of formula R^{3b} is substituted by R^{18}, R^{19} and R^{20};

G, G^1 and G^2 are taken separately and are each hydrogen and R^6 is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; R^7 and R^8 are each independently hydrogen or (C_1-C_4)alkyl; or

G and G^1 are taken together and are (C_1-C_3)alkylene and R^6, R^7, R^8 and G^2 are hydrogen; or

G^1 and G^2 are taken together and are (C_1-C_3)alkylene and R^6, R^7, R^8 and G are hydrogen;

q is 0 or 1;

X is a covalent bond, -(C=NR^{10})-, oxycarbonyl, vinylenylcarbonyl, oxy(C_1-C_4)alkylenylcarbonyl, (C_1-C_4)alkylenylcarbonyl, (C_3-C_4)alkenylcarbonyl, thio(C_1-C_4)alkylenylcarbonyl, vinylenylsulfonyl, sulfinyl-(C_1-C_4)alkylenylcarbonyl, sulfonyl-(C_1-C_4)alkylenylcarbonyl or carbonyl(C_0-C_4)alkylenylcarbonyl; wherein said oxy(C_1-C_4)alkylenylcarbonyl, (C_1-C_4)alkylenylcarbonyl, (C_3-C_4)alkenylcarbonyl and thio(C_1-C_4)alkylenylcarbonyl in the definition of X are each optionally and independently substituted with up to two (C_1-C_4)alkyl, benzyl or Ar; said vinylenylsulfonyl and said vinylenylcarbonyl in the definition of X are optionally substituted independently on one or two vinylenyl carbons with (C_1-C_4)alkyl, benzyl or Ar; and said carbonyl(C_0-C_4)alkylenylcarbonyl in the definition of X is optionally substituted indepedently with up to three (C_1-C_4)alkyl, benzyl or Ar;

R^{10} is hydrogen or (C_1-C_4)alkyl;

R^9 is (C_3-C_7)cycloalkyl, Ar^1-(C_0-C_3)alkylenyl or (C_1-C_6)alkyl optionally substituted with up to five fluoro; provided that when q = 0 and X is a covalent bond, oxycarbonyl or (C_1-C_4)alkylenylcarbonyl, then R^9 is not (C_1-C_6)alkyl;

Ar and Ar^1 are independently a fully saturated, partially saturated or fully unsaturated five- to eight-membered ring optionally having up to four heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or fully unsaturated five- to seven-membered rings, taken independently, optionally having up to four heteroatoms selected independently from nitrogen, sulfur and oxygen, or a tricyclic ring consisting of three fused independently partially saturated, fully saturated or fully

unsaturated five to seven membered rings, taken independently, optionally having up to four heteroatoms selected independently from nitrogen, sulfur and oxygen, said partially saturated, fully saturated ring or fully unsaturated monocyclic ring, bicyclic ring or tricyclic ring optionally having one or two oxo groups substituted on carbon or one or two oxo groups substituted on sulfur;

Ar and Ar^1 are optionally independently substituted on carbon or nitrogen, on one ring if the moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with up to a total of four substituents independently selected from R^{11}, R^{12}, R^{13} and R^{14}; wherein R^{11}, R^{12}, R^{13} and R^{14} are each taken separately and are each independently halo, formyl, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylenyloxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, C(OH)$R^{15}R^{16}$, naphthyl, phenyl, imidazolyl, pyridyl, triazolyl, morpholinyl, (C_0-C_4)alkylsulfamoyl, N-(C_0-C_4)alkylcarbamoyl, N,N-di-(C_1-C_4)alkylcarbamoyl, N-phenylcarbamoyl, N-(C_1-C_4)alkyl-N-phenylcarbamoyl, N,N-diphenyl carbamoyl, (C_1-C_4)alkylcarbonylamido, (C_3-C_7)cycloalkylcarbonylamido, phenylcarbonylamido, piperidinyl, pyrrolidinyl, piperazinyl, cyano, benzimidazolyl, amino, anilino, pyrimidyl, oxazolyl, isoxazolyl, tetrazolyl, thienyl, thiazolyl, benzothiazolyl, pyrrolyl, pyrazolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfanyl, furanyl, 8-(C_1-C_4)alkyl-3,8-diaza[3.2.1]bicyclooctyl, 3,5-dioxo-1,2,4-triazinyl, phenoxy, thiophenoxy, (C_1-C_4)alkylsulfanyl, (C_1-C_4)alkylsulfonyl, (C_3-C_7)cycloalkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said naphthyl, phenyl, pyridyl, piperidinyl, benzimidazolyl, pyrimidyl, thienyl, benzothiazolyl, pyrrolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfanyl, furanyl, thiophenoxy, anilino and phenoxy in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to two substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with up to two substituents independently selected from (C_1-C_4)alkyl; said pyrrolidinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is

optionally substituted with up to two substituents independently selected from hydroxy, hydroxy-(C_1-C_3)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with up to three substituents independently selected from (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_3)alkyl, phenyl, pyridyl, (C_0-C_4)alkylsulfamoyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said triazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said tetrazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with hydroxy-(C_2-C_3)alkyl or (C_1-C_4)alkyl optionally substituted with up to five fluoro; and said phenyl and pyridyl which are optionally substituted on piperazine in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; or

R^{11} and R^{12} are taken together on adjacent carbon atoms and are $-CH_2OC(CH_3)_2OCH_2-$ or $-O-(CH_2)_p-O-$, and R^{13} and R^{14} are taken separately and are each independently hydrogen or (C_1-C_4)alkyl;

p is 1, 2 or 3;

R^{15} and R^{16} are taken separately and are each independently hydrogen, (C_1-C_4)alkyl optionally substituted with up to five fluoro; or R^{15} and R^{16} are taken separately and R^{15} is hydrogen and R^{16} is (C_3-C_6)cycloalkyl, hydroxy-(C_1-C_3)alkyl, phenyl, pyridyl, pyrimidyl, thienyl, furanyl, thiazolyl, oxazolyl, imidazolyl, benzothiazolyl or benzoxazolyl; or R^{15} and R^{16} are taken together and are (C_3-C_6)alkylene;

G^3, G^4 and G^5 are taken separately and are each hydrogen; r is 0; R^{18} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; and R^{19} and R^{20} are each independently (C_1-C_4)alkyl; or

G^3, G^4 and G^5 are taken separately and are each hydrogen; r is 1; R^{18} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl

or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; and

R^{19} and R^{20} are each independently hydrogen or (C_1-C_4)alkyl; or

G^3 and G^4 are taken together and are (C_1-C_3)alkylene; r is 0 or 1; and R^{18}, R^{19}, R^{20} and G^5 are hydrogen; or

G^4 and G^5 are taken together and are (C_1-C_3)alkylene; r is 0 or 1; and R^{18}, R^{19}, R^{20} and G^3 are hydrogen;

R^{17} is $SO_2NR^{21}R^{22}$, $CONR^{21}R^{22}$, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylcarbonyl, Ar^2-carbonyl, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkylsulfinyl, Ar^2-sulfonyl, Ar^2-sufinyl and (C_1-C_6)alkyl;

R^{21} and R^{22} are taken separately and are each independently selected from hydrogen, (C_1-C_6)alkyl, (C_3-C_7)cycloalkyl and Ar^2-(C_0-C_4)alkylenyl; or

R^{21} and R^{22} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl, 1,2,3,4-tetrahydro-isoquinolyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{21} and R^{22} is optionally substituted independently with one substituent selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrrolidinyl, piperidinyl, azepinyl in the definition of R^{21} and R^{22} are optionally substituted independently with up to two substituents independently selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{21} and R^{22} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl in the definition of R^{21} and R^{22} is optionally substituted independently with up to three substituents independently selected from phenyl, pyridyl, pyrimidyl, (C_1-C_4)alkoxycarbonyl and (C_1-C_4)alkyl optionally substituted with up to five fluoro; said 1,2,3,4-tetrahydro-isoquinolyl and said 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl in the definition of R^{21} and R^{22} are optionally substituted independently with up to three

substituents independently selected from hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{21} and R^{22} is optionally substituted with up to four substituents independently selected from hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrimidyl, pyridyl and phenyl which are optionally substituted on said piperazine in the definition of R^{21} and R^{22} is optionally substituted with up to three substituents selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

Ar^2 is independently defined as set forth for Ar and Ar^1 above;

said Ar^2 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{23} is $CONR^{25}R^{26}$ or $SO_2R^{25}R^{26}$, wherein R^{25} is hydrogen (C_1-C_4)alkyl or Ar^3-(C_0-C_4)alkylenyl and R^{26} is Ar^3-(C_0-C_4)alkylenyl; provided that when Ar^3 is phenyl, naphthyl or biphenyl, then R^{23} cannot be $CONR^{25}R^{26}$ where R^{25} is hydrogen or Ar^3 and R^{26} is Ar^3;

R^{24} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro;

Ar^3 is independently defined as set forth for Ar and Ar^1 above;

said Ar^3 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{27} is hydrogen or (C_1-C_4)alkyl;

R^{28} and R^{29} are each independently hydrogen, hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro, (C_1-C_4)alkoxy optionally substituted with up to five fluoro, phenyl, pyridyl, pyrimidyl, thienyl, furanyl, thiazolyl, oxazolyl, phenoxy, thiophenoxy, $SO_2NR^{30}R^{31}$, $CONR^{30}R^{31}$ or $NR^{30}R^{31}$; said thienyl, pyrimidyl, furanyl, thiazolyl and oxazolyl in the definition of R^{28} and R^{29} are optionally substituted by up to two hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said phenyl, pyridyl, phenoxy and thiophenoxy in the definition of R^{28} and R^{29} are optionally substituted by

up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

R^{30} and R^{31} are each independently hydrogen, (C_1-C_4)alkyl, (C_3-C_7)cycloalkyl or phenyl, said phenyl is optionally substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; or

R^{30} and R^{31} are taken together with the nitrogen to which they are attached to form indolinyl, pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl; said pyrrolidinyl and piperidinyl in the definition of R^{30} and R^{31} are optionally substituted with up to two hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said indolinyl and piperazinyl in the definition of R^{30} and R^{31} are optionally substituted with up to three hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{30} and R^{31} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

A is N optionally substituted with hydrogen or (C_1-C_4)alkyl and B is carbonyl; or

A is carbonyl and B is N optionally substituted with hydrogen or (C_1-C_4)alkyl;

R^{32} is hydrogen or (C_1-C_4)alkyl;

R^{33} is phenyl, pyridyl, pyrimidyl, thiazolyl, oxazolyl, benzyl, quinolyl, isoquinolyl, phthalizinyl, quinoxanlyl, benzothiazoyl, benzoxazolyl, benzofuranyl or benzothienyl; said phenyl, pyridyl, pyrimidyl, thiazolyl, oxazolyl, benzyl, quinolyl, isoquinolyl, phthalizinyl, quinoxanlyl, benzothiazoyl, benzoxazolyl, benzofuranyl and benzothienyl in the definition of R^{33} are optionally substituted with up to three phenyl, phenoxy, $NR^{34}R^{35}$, halo, hydroxy, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

R^{34} and R^{35} are each independently hydrogen, (C_1-C_4 alkyl), phenyl or phenylsulfonyl; said phenyl and phenylsulfonyl in the definition of R^{34} and R^{35} are optionally substituted with up to three halo, hydroxy, (C_1-C_4)alkyl optionally

substituted with up to five fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro;

D is CO, CHOH or CH_2;

E is O, NH or S;

R^{36} and R^{37} are taken separately and are each independently hydrogen, halo, cyano, hydroxy, amino, $(C_1$-$C_6)$alkylamino, di-$(C_1$-$C_6)$alkylamino, pyrrolidino, piperidino, morpholino, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, hydroxy-$(C_1$-$C_4)$alkyl, Ar^4, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro;

R^{38}, R^{39} and R^{40} are each independently hydrogen or $(C_1$-$C_4)$-alkyl;

Ar^4 is phenyl, furanyl, thienyl, pyridyl, pyrimidyl, pyrazinyl or pyridazinyl; said Ar^4 being optionally substituted with up to three hydroxy, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; or

R^{36} and R^{37} are taken together on adjacent carbon atoms and are -O-$(CH_2)_t$-O-;

t is 1, 2 or 3;

Y is $(C_2$-$C_6)$alkylene;

R^{44}, R^{45} and R^{46} are each independently hydrogen or $(C_1$-$C_4)$alkyl;

m and n are each independently 1, 2 or 3, provided that the sum of m and n is 2, 3 or 4;

k is 0, 1, 2, 3 or 4;

Y^1 is a covalent bond, carbonyl, sulfonyl or oxycarbonyl;

R^{43} is $(C_3$-$C_7)$cycloalkyl, Ar^5-$(C_0$-$C_4)$alkylenyl, $NR^{47}R^{48}$ or $(C_1$-$C_6)$alkyl optionally substituted with one to five fluoro; provided that when Y^1 is a covalent bond or oxycarbonyl, then R^{43} is not $NR^{47}R^{48}$;

R^{47} and R^{48} are taken separately and are each independently selected from hydrogen, Ar^5, $(C_1$-$C_6)$alkyl and Ar^5-$(C_0$-$C_4)$alkylenyl; or

R^{47} and R^{48} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 1,2,3,4-tetrahydroisoquinolyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{47} and R^{48} are optionally substituted with one hydroxy, amino, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said pyrrolidinyl, piperidinyl and azepinyl in the definition of R^{47} and R^{48} are

optionally substituted with up to two hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{47} and R^{48} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl, 1,2,3,4-tetrahydroisoquinolyl and 5,6,7,8-tetrahydro[4,3-d]pyrimidyl in the definition of R^{47} and R^{48} are optionally substituted with up to three hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{47} and R^{48} are optionally substituted with up to four hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

Ar^5 is independently defined as set forth for Ar and Ar^1 above;

Ar^5 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{42} and R^{42a} are independently hydrogen, (C_3-C_7)cycloalkyl, Ar^6-(C_0-C_3)alkylenyl, Ar^6-(C_2-C_4)alkenyl, Ar^6-carbonyl or (C_1-C_6)alkyl optionally substituted with up to five fluoro;

Ar^6 is independently defined as set forth for Ar and Ar^1 above;

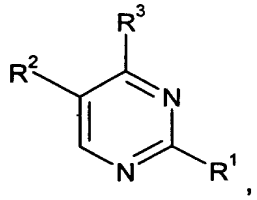
Ar^6 is optionally independently substituted as set forth for Ar and Ar^1 above; and

R^{41} and R^{41a} are each independently hydrogen or (C_1-C_4)alkyl.

166. A compound of claim 165 selected from 1R-(4-{4-[2-(1R-butyryloxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethyl butyrate; 1R-(4-{4-[2-(1S-butyryloxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethyl butyrate; 1S-(4-{4-[2-(1R-butyryloxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethyl butyrate; (E)-1R-{4-[4-(2-methyl-32-phenyl-acryloyl)-piperazin-1-yl]-pyrimidin-2-yl}-ethyl acetate; (R)-1-[4-(4-quinoxalin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethyl acetate; 1R-(4-{4-[2-(1RS-hydroxy-ethyl)-pyrimidin-4-yl]-2R,6S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethyl butyrate; 1RS-(4-{4-[2-(1R-hydroxy-ethyl)-pyrimidin-4-yl]-3R,5S-dimethyl-piperazin-1-yl}-pyrimidin-2-yl)-ethyl butyrate; 1R-[4-(3S-methyl-4-oxazolo[5,4-b]pyridin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethyl butyrate; 1R-{4-[3R,5S-dimethyl-4-(4-methyl-6-phenyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethyl butyrate; 1R-{4-[4-(4-

cyclopropyl-[1,3,5]triazin-2-yl)-3R,5S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethyl butyrate; 1R-{4-[4-(4-cyclopropyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethyl butyrate; 1R-{4-[4-(4,6-dimethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethyl butyrate; 1R-{4-[4-(4-hydroxymethyl-6-phenyl-[1,3,5]triazin-2-yl)-2R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethyl butyrate; 1R-{4-[4-(4-methoxy-6-methoxymethyl-[1,3,5]triazin-2-yl)-R,6S-dimethyl-piperazin-1-yl]-pyrimidin-2-yl}-ethyl butyrate; and 1R-{4-[2R,6S-dimethyl-4-(4-methyl-[1,3,5]triazin-2-yl)-piperazin-1-yl]-pyrimidin-2-yl}-ethyl butyrate.

167. A compound of the formula I^B,



I^B

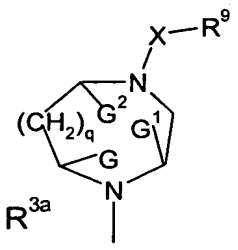
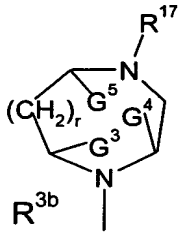
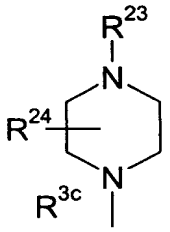
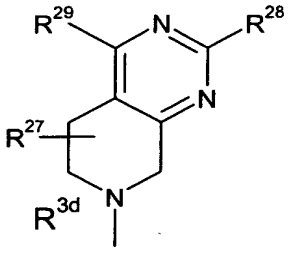
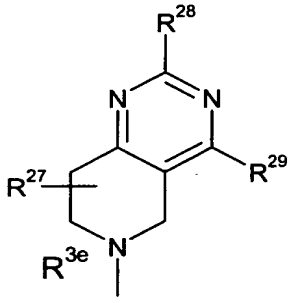
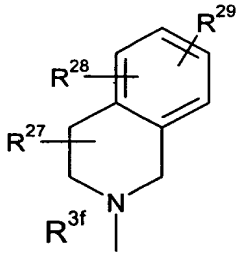
wherein:

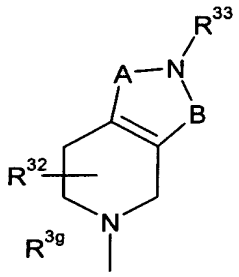
R^1 is C-(OR^{81})R^4R^5, where R^{81} is an acyl radical of a carboxylic acid aldose reductase inhibitor;

R^4 and R^5 are each independently hydrogen, methyl, ethyl or hydroxy-(C_1-C_3)alkyl;

R^2 is hydrogen, (C_1-C_4)alkyl or (C_1-C_4)alkoxy;

R^3 is a radical of the formula


X
R9
N
G2
(CH2)q
G1
G
N
R3a
,

R17
N
G5
(CH2)r
G4
G3
N
R3b
,

R23
N
R24
N
R3c
,

R29
N
R28
N
R27
N
R3d
,

R28
N
N
R27
R29
N
R3e
,

R29
R28
R27
N
R3f
,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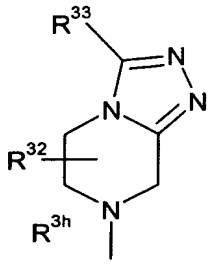
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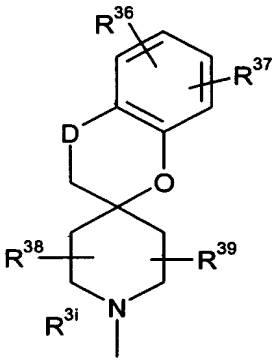
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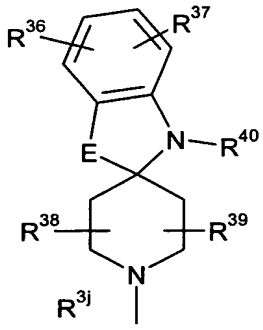
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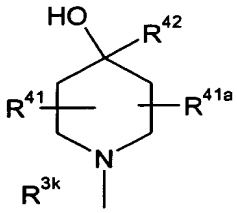
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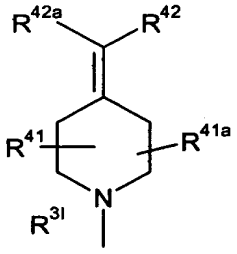
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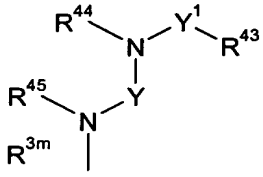
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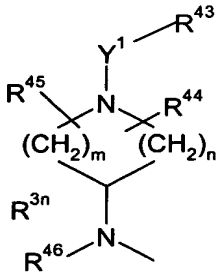
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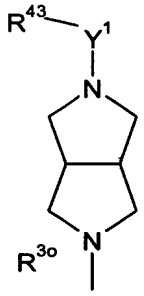
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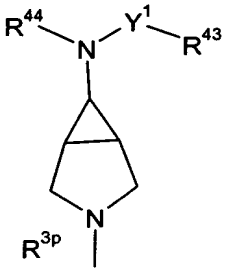
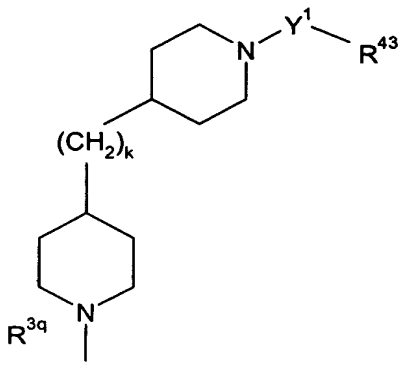

or

;

wherein said radical of formula R^{3a} is substituted by R^6, R^7 and R^8;

said radical of formula R^{3b} is substituted by R^{18}, R^{19} and R^{20};

G, G^1 and G^2 are taken separately and are each hydrogen and R^6 is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; R^7 and R^8 are each independently hydrogen or (C_1-C_4)alkyl; or

G and G^1 are taken together and are (C_1-C_3)alkylene and R^6, R^7, R^8 and G^2 are hydrogen; or

G^1 and G^2 are taken together and are (C_1-C_3)alkylene and R^6, R^7, R^8 and G are hydrogen;

q is 0 or 1;

X is a covalent bond, -(C=NR^{10})-, oxycarbonyl, vinylenylcarbonyl, oxy(C_1-C_4)alkylenylcarbonyl, (C_1-C_4)alkylenylcarbonyl, (C_3-C_4)alkenylcarbonyl, thio(C_1-C_4)alkylenylcarbonyl, vinylenylsulfonyl, sulfinyl-(C_1-C_4)alkylenylcarbonyl, sulfonyl-(C_1-C_4)alkylenylcarbonyl or carbonyl(C_0-C_4)alkylenylcarbonyl; wherein said oxy(C_1-C_4)alkylenylcarbonyl, (C_1-C_4)alkylenylcarbonyl, (C_3-C_4)alkenylcarbonyl and thio(C_1-C_4)alkylenylcarbonyl in the definition of X are each optionally and independently substituted with up to two (C_1-C_4)alkyl, benzyl or Ar; said vinylenylsulfonyl and said vinylenylcarbonyl in the definition of X are optionally substituted independently on one or two vinylenyl carbons with (C_1-C_4)alkyl, benzyl or Ar; and said carbonyl(C_0-C_4)alkylenylcarbonyl in the definition of X is optionally substituted indepedently with up to three (C_1-C_4)alkyl, benzyl or Ar;

R^{10} is hydrogen or (C_1-C_4)alkyl;

R^9 is (C_3-C_7)cycloalkyl, Ar^1-(C_0-C_3)alkylenyl or (C_1-C_6)alkyl optionally substituted with up to five fluoro; provided that when q = 0 and X is a covalent bond, oxycarbonyl or (C_1-C_4)alkylenylcarbonyl, then R^9 is not (C_1-C_6)alkyl;

Ar and Ar^1 are independently a fully saturated, partially saturated or fully unsaturated five- to eight-membered ring optionally having up to four heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or fully unsaturated five- to seven-membered rings, taken independently, optionally having up to four heteroatoms selected independently from nitrogen, sulfur and oxygen, or a tricyclic ring consisting of three fused independently partially saturated, fully saturated or fully

unsaturated five to seven membered rings, taken independently, optionally having up to four heteroatoms selected independently from nitrogen, sulfur and oxygen, said partially saturated, fully saturated ring or fully unsaturated monocyclic ring, bicyclic ring or tricyclic ring optionally having one or two oxo groups substituted on carbon or one or two oxo groups substituted on sulfur;

Ar and Ar^1 are optionally independently substituted on carbon or nitrogen, on one ring if the moiety is monocyclic, on one or both rings if the moiety is bicyclic, or on one, two or three rings if the moiety is tricyclic, with up to a total of four substituents independently selected from R^{11}, R^{12}, R^{13} and R^{14}; wherein R^{11}, R^{12}, R^{13} and R^{14} are each taken separately and are each independently halo, formyl, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylenyloxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, $C(OH)R^{15}R^{16}$, naphthyl, phenyl, imidazolyl, pyridyl, triazolyl, morpholinyl, (C_0-C_4)alkylsulfamoyl, N-(C_0-C_4)alkylcarbamoyl, N,N-di-(C_1-C_4)alkylcarbamoyl, N-phenylcarbamoyl, N-(C_1-C_4)alkyl-N-phenylcarbamoyl, N,N-diphenyl carbamoyl, (C_1-C_4)alkylcarbonylamido, (C_3-C_7)cycloalkylcarbonylamido, phenylcarbonylamido, piperidinyl, pyrrolidinyl, piperazinyl, cyano, benzimidazolyl, amino, anilino, pyrimidyl, oxazolyl, isoxazolyl, tetrazolyl, thienyl, thiazolyl, benzothiazolyl, pyrrolyl, pyrazolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfanyl, furanyl, 8-(C_1-C_4)alkyl-3,8-diaza[3.2.1]bicyclooctyl, 3,5-dioxo-1,2,4-triazinyl, phenoxy, thiophenoxy, (C_1-C_4)alkylsulfanyl, (C_1-C_4)alkylsulfonyl, (C_3-C_7)cycloalkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said naphthyl, phenyl, pyridyl, piperidinyl, benzimidazolyl, pyrimidyl, thienyl, benzothiazolyl, pyrrolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfanyl, furanyl, thiophenoxy, anilino and phenoxy in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to two substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with up to two substituents independently selected from (C_1-C_4)alkyl; said pyrrolidinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is

optionally substituted with up to two substituents independently selected from hydroxy, hydroxy-(C_1-C_3)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with up to three substituents independently selected from (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_3)alkyl, phenyl, pyridyl, (C_0-C_4)alkylsulfamoyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said triazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said tetrazolyl in the definition of R^{11}, R^{12}, R^{13} and R^{14} is optionally substituted with hydroxy-(C_2-C_3)alkyl or (C_1-C_4)alkyl optionally substituted with up to five fluoro; and said phenyl and pyridyl which are optionally substituted on piperazine in the definition of R^{11}, R^{12}, R^{13} and R^{14} are optionally substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; or

R^{11} and R^{12} are taken together on adjacent carbon atoms and are $-CH_2OC(CH_3)_2OCH_2-$ or $-O-(CH_2)_p-O-$, and R^{13} and R^{14} are taken separately and are each independently hydrogen or (C_1-C_4)alkyl;

p is 1, 2 or 3;

R^{15} and R^{16} are taken separately and are each independently hydrogen, (C_1-C_4)alkyl optionally substituted with up to five fluoro; or R^{15} and R^{16} are taken separately and R^{15} is hydrogen and R^{16} is (C_3-C_6)cycloalkyl, hydroxy-(C_1-C_3)alkyl, phenyl, pyridyl, pyrimidyl, thienyl, furanyl, thiazolyl, oxazolyl, imidazolyl, benzothiazolyl or benzoxazolyl; or R^{15} and R^{16} are taken together and are (C_3-C_6)alkylene;

G^3, G^4 and G^5 are taken separately and are each hydrogen; r is 0; R^{18} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; and R^{19} and R^{20} are each independently (C_1-C_4)alkyl; or

G^3, G^4 and G^5 are taken separately and are each hydrogen; r is 1; R^{18} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl

or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro; and

R^{19} and R^{20} are each independently hydrogen or (C_1-C_4)alkyl; or

G^3 and G^4 are taken together and are (C_1-C_3)alkylene; r is 0 or 1; and R^{18}, R^{19}, R^{20} and G^5 are hydrogen; or

G^4 and G^5 are taken together and are (C_1-C_3)alkylene; r is 0 or 1; and R^{18}, R^{19}, R^{20} and G^3 are hydrogen;

R^{17} is $SO_2NR^{21}R^{22}$, $CONR^{21}R^{22}$, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylcarbonyl, Ar^2-carbonyl, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkylsulfinyl, Ar^2-sulfonyl, Ar^2-sufinyl and (C_1-C_6)alkyl;

R^{21} and R^{22} are taken separately and are each independently selected from hydrogen, (C_1-C_6)alkyl, (C_3-C_7)cycloalkyl and Ar^2-(C_0-C_4)alkylenyl; or

R^{21} and R^{22} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl, 1,2,3,4-tetrahydro-isoquinolyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{21} and R^{22} is optionally substituted independently with one substituent selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrrolidinyl, piperidinyl, azepinyl in the definition of R^{21} and R^{22} are optionally substituted independently with up to two substituents independently selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{21} and R^{22} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl in the definition of R^{21} and R^{22} is optionally substituted independently with up to three substituents independently selected from phenyl, pyridyl, pyrimidyl, (C_1-C_4)alkoxycarbonyl and (C_1-C_4)alkyl optionally substituted with up to five fluoro; said 1,2,3,4-tetrahydro-isoquinolyl and said 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl in the definition of R^{21} and R^{22} are optionally substituted independently with up to three

substituents independently selected from hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{21} and R^{22} is optionally substituted with up to four substituents independently selected from hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrimidyl, pyridyl and phenyl which are optionally substituted on said piperazine in the definition of R^{21} and R^{22} is optionally substituted with up to three substituents selected from hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

Ar^2 is independently defined as set forth for Ar and Ar^1 above;

said Ar^2 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{23} is $CONR^{25}R^{26}$ or $SO_2R^{25}R^{26}$, wherein R^{25} is hydrogen (C_1-C_4)alkyl or Ar^3-(C_0-C_4)alkylenyl and R^{26} is Ar^3-(C_0-C_4)alkylenyl; provided that when Ar^3 is phenyl, naphthyl or biphenyl, then R^{23} cannot be $CONR^{25}R^{26}$ where R^{25} is hydrogen or Ar^3 and R^{26} is Ar^3;

R^{24} is hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl or phenyl optionally independently substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl or (C_1-C_4)alkoxy, wherein said (C_1-C_4)alkyl in the definition of R^6 and said (C_1-C_4)alkoxy in the definition of R^6 are optionally and independently substituted with up to five fluoro;

Ar^3 is independently defined as set forth for Ar and Ar^1 above;

said Ar^3 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{27} is hydrogen or (C_1-C_4)alkyl;

R^{28} and R^{29} are each independently hydrogen, hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro, (C_1-C_4)alkoxy optionally substituted with up to five fluoro, phenyl, pyridyl, pyrimidyl, thienyl, furanyl, thiazolyl, oxazolyl, phenoxy, thiophenoxy, $SO_2NR^{30}R^{31}$, $CONR^{30}R^{31}$ or $NR^{30}R^{31}$; said thienyl, pyrimidyl, furanyl, thiazolyl and oxazolyl in the definition of R^{28} and R^{29} are optionally substituted by up to two hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said phenyl, pyridyl, phenoxy and thiophenoxy in the definition of R^{28} and R^{29} are optionally substituted by

up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

R^{30} and R^{31} are each independently hydrogen, (C_1-C_4)alkyl, (C_3-C_7)cycloalkyl or phenyl, said phenyl is optionally substituted with up to three hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; or

R^{30} and R^{31} are taken together with the nitrogen to which they are attached to form indolinyl, pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl; said pyrrolidinyl and piperidinyl in the definition of R^{30} and R^{31} are optionally substituted with up to two hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said indolinyl and piperazinyl in the definition of R^{30} and R^{31} are optionally substituted with up to three hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxycarbonyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{30} and R^{31} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

A is N optionally substituted with hydrogen or (C_1-C_4)alkyl and B is carbonyl; or

A is carbonyl and B is N optionally substituted with hydrogen or (C_1-C_4)alkyl;

R^{32} is hydrogen or (C_1-C_4)alkyl;

R^{33} is phenyl, pyridyl, pyrimidyl, thiazolyl, oxazolyl, benzyl, quinolyl, isoquinolyl, phthalizinyl, quinoxanlyl, benzothiazoyl, benzoxazolyl, benzofuranyl or benzothienyl; said phenyl, pyridyl, pyrimidyl, thiazolyl, oxazolyl, benzyl, quinolyl, isoquinolyl, phthalizinyl, quinoxanlyl, benzothiazoyl, benzoxazolyl, benzofuranyl and benzothienyl in the definition of R^{33} are optionally substituted with up to three phenyl, phenoxy, $NR^{34}R^{35}$, halo, hydroxy, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

R^{34} and R^{35} are each independently hydrogen, (C_1-C_4 alkyl), phenyl or phenylsulfonyl; said phenyl and phenylsulfonyl in the definition of R^{34} and R^{35} are optionally substituted with up to three halo, hydroxy, (C_1-C_4)alkyl optionally

substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

D is CO, CHOH or CH_2;

E is O, NH or S;

R^{36} and R^{37} are taken separately and are each independently hydrogen, halo, cyano, hydroxy, amino, (C_1-C_6)alkylamino, di-(C_1-C_6)alkylamino, pyrrolidino, piperidino, morpholino, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl, Ar^4, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

R^{38}, R^{39} and R^{40} are each independently hydrogen or (C_1-C_4)-alkyl;

Ar^4 is phenyl, furanyl, thienyl, pyridyl, pyrimidyl, pyrazinyl or pyridazinyl; said Ar^4 being optionally substituted with up to three hydroxy, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; or

R^{36} and R^{37} are taken together on adjacent carbon atoms and are -O-$(CH_2)_t$-O-;

t is 1, 2 or 3;

Y is (C_2-C_6)alkylene;

R^{44}, R^{45} and R^{46} are each independently hydrogen or (C_1-C_4)alkyl;

m and n are each independently 1, 2 or 3, provided that the sum of m and n is 2, 3 or 4;

k is 0, 1, 2, 3 or 4;

Y^1 is a covalent bond, carbonyl, sulfonyl or oxycarbonyl;

R^{43} is (C_3-C_7)cycloalkyl, Ar^5-(C_0-C_4)alkylenyl, $NR^{47}R^{48}$ or (C_1-C_6)alkyl optionally substituted with one to five fluoro; provided that when Y^1 is a covalent bond or oxycarbonyl, then R^{43} is not $NR^{47}R^{48}$;

R^{47} and R^{48} are taken separately and are each independently selected from hydrogen, Ar^5, (C_1-C_6)alkyl and Ar^5-(C_0-C_4)alkylenyl; or

R^{47} and R^{48} are taken together with the nitrogen atom to which they are attached to form azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, azepinyl, azabicyclo[3.2.2]nonanyl, azabicyclo[2.2.1]heptyl, 1,2,3,4-tetrahydroisoquinolyl, 6,7-dihydro-5H-dibenzo[c,e]azepinyl or 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidyl; said azetidinyl in the definition of R^{47} and R^{48} are optionally substituted with one hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said pyrrolidinyl, piperidinyl and azepinyl in the definition of R^{47} and R^{48} are

optionally substituted with up to two hydroxy, amino, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said morpholinyl in the definition of R^{47} and R^{48} is optionally substituted with up to two substituents independently selected from hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said piperazinyl, 1,2,3,4-tetrahydroisoquinolyl and 5,6,7,8-tetrahydro[4,3-d]pyrimidyl in the definition of R^{47} and R^{48} are optionally substituted with up to three hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; and said 6,7-dihydro-5H-dibenzo[c,e]azepinyl in the definition of R^{47} and R^{48} are optionally substituted with up to four hydroxy, amino, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro;

Ar^5 is independently defined as set forth for Ar and Ar^1 above;

Ar^5 is optionally independently substituted as set forth for Ar and Ar^1 above;

R^{42} and R^{42a} are independently hydrogen, (C_3-C_7)cycloalkyl, Ar^6-(C_0-C_3)alkylenyl, Ar^6-(C_2-C_4)alkenyl, Ar^6-carbonyl or (C_1-C_6)alkyl optionally substituted with up to five fluoro;

Ar^6 is independently defined as set forth for Ar and Ar^1 above;

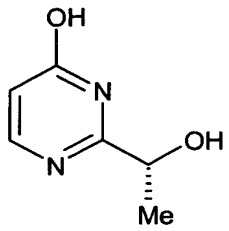
Ar^6 is optionally independently substituted as set forth for Ar and Ar^1 above; and

R^{41} and R^{41a} are each independently hydrogen or (C_1-C_4)alkyl.

168. A compound of claim 167 wherein R^{81} is the acyl radical of ponalrestat, tolrestat, zenarastat, zopolrestat, epalrestat, ZD5522 or sorbinil.

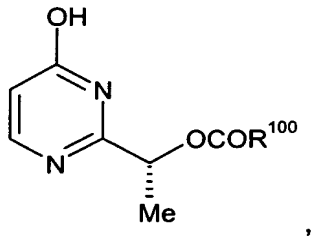
169. A compound selected from (E)-[4-oxo-3-(5-trifluoromethyl-benzothiazol-2-ylmethyl)-3,4-dihydro-phthalazin-1-yl]-acetic acid 1R-[4-(4-quinoxalin-2-yl-piperazin-1-yl)-pyrimidin-2-yl]-ethyl ester and (E)-[4-Oxo-3-(5-trifluoromethyl-benzothiazol-2-ylmethyl)-3,4-dihydro-phthalazin-1-yl]-acetic acid 1R-{4-[4-(3-thiophen-2-yl-acryloyl)-piperazin-1-yl]-pyrimidin-2-yl}-ethyl ester.

170. A compound of the formula Z



Z

171. A compound of the formula ZZ,



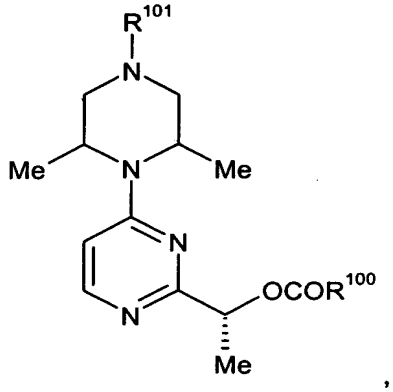
ZZ

wherein R^{100} is $(C_1\text{-}C_8)$alkyl, benzyl or phenyl wherein said benzyl and phenyl are optionally substituted with up to three halo or $(C_1\text{-}C_4)$alkyl.

172. A compound of claim 171 wherein R^{100} is $(C_1\text{-}C_4)$alkyl.

173. A compound of claim 172 wherein R^{100} is n-butyl or ethyl.

174. A compound of the formula III,



III

wherein:

R^{100} is $(C_1\text{-}C_8)$alkyl, benzyl or phenyl wherein said benzyl and phenyl are optionally substituted with up to three halo or $(C_1\text{-}C_4)$alkyl; and

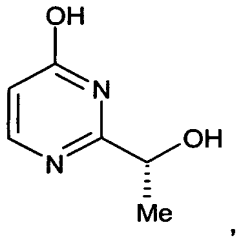
R^{101} is hydrogen or a suitable amine protecting group.

175. A compound of claim 174 wherein R^{100} is $(C_1\text{-}C_4)$alkyl and R^{101} is benzyl or tert-butyloxycarbonyl.

176. A compound of claim 175 wherein R^{100} is n-butyl or ethyl and R^{101} is benzyl.

177. A compound of claim 175 wherein R^{100} is n-butyl or ethyl and R^{101} is tert-butyloxycarbonyl.

178. A process for preparing a compound of the formula Z,



Z

comprising:

a) reacting R-(+)-2-hydroxy-propionamide with triethyloxonium tetrafluoroborate in a reaction inert solvent for 10 minutes to 24 hours at 0 °C to ambient temperature to form the corresponding imidate;

b) reacting said corresponding imidate with anhydrous ammonia in a reaction inert solvent for 2 hours to 24 hours at 0 °C to ambient temperature to form R-(+)-2-hydroxy-propionamidine hydrochloride; and

c) reacting said R-(+)-2-hydroxy-propionamidine hydrochloride with ethyl 3-hydroxy-acrylate sodium salt and a suitable base in a reaction inert solvent to form said compound of formula Z.

179. A pharmaceutical composition comprising a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said prodrug or said compound, and a glycogen phosphorylase inhibitor (GPI), a prodrug of said GPI or a pharmaceutically acceptable salt of said GPI or said prodrug.

180. A kit comprising:

a. a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said prodrug or said compound in a first unit dosage form;

b. a glycogen phosphorylase inhibitor (GPI), a prodrug thereof or a pharmaceutically acceptable salt of said prodrug or said GPI in a second unit dosage form; and

c. a container.

181. A method of treating or preventing diabetic complications in a mammal comprising administering to said mammal a pharmaceutical composition of claim 179.

182. A method of treating hyperglycemia in a mammal comprising administering to said mammal a pharmaceutical composition of claim 179.

183. A method of treating ischemia in a mammal suffering from ischemia comprising administering to said mammal a pharmaceutical composition of claim 179.

184. A method of treating diabetes in a mammal comprising adminstering to said mammal a pharmaceutical composition of claim 179.

185. A method of treating diabetic complications in a mammal comprising adminstering to said mammal a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and a glycogen phosphorylase inhibitor (GPI), a prodrug of said GPI or a pharmaceutically acceptable salt of said GPI or said prodrug.

186. A method of treating hyperglycemia in a mammal comprising administering to said mammal a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and a glycogen phosphorylase inhibitor (GPI), a prodrug of said GPI or a pharmaceutically acceptable salt of said GPI or said prodrug.

187. A method of treating ischemia in a mammal comprising adminstering to said mammal a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and a glycogen phosphorylase inhibitor (GPI), a prodrug of said GPI or a pharmaceutically acceptable salt of said GPI or said prodrug.

188. A method of treating diabetes in a mammal comprising administering to said mammal a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug and a glycogen phosphorylase inhibitor (GPI), a prodrug of said GPI or a pharmaceutically acceptable salt of said GPI or said prodrug.